

(19) World Intellectual Property Organization
International Bureau



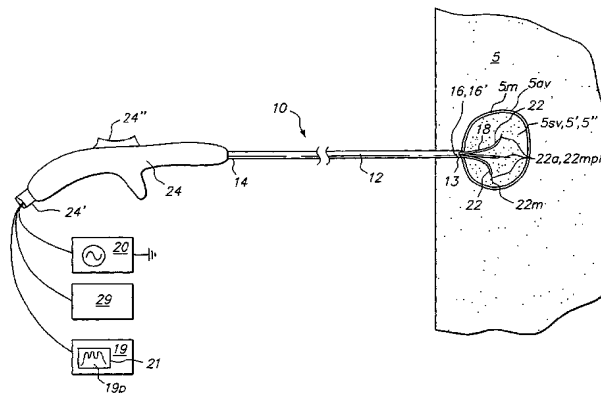
(43) International Publication Date
25 April 2002 (25.04.2002)

PCT

(10) International Publication Number
WO 02/32335 A1

- (51) International Patent Classification⁷: **A61B 18/14** (74) Agent: **HARRIS, Joel**; Rita Medical Systems, 967 Shoreline Blvd, Mountain View, CA 94043 (US).
- (21) International Application Number: PCT/US01/23553
- (22) International Filing Date: 25 July 2001 (25.07.2001)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
60/220,639 25 July 2000 (25.07.2000) US
- (71) Applicant (for all designated States except US): **RITA MEDICAL SYSTEMS INC.** [US/US]; 967 N. Shoreline Blvd, Mountain View, CA 94043 (US).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): **JOHNSON, Theodore** [US/US]; 784 Carolina Street, San Francisco, Ca 94107 (US). **BALBIERZ, Daniel** [US/US]; 973 Cambridge Drive, Redwood City, CA 94061 (US). **PEARSON, Robert** [US/US]; 4694 La Crescent Loop, San Jose, CA 95136 (US).
- (81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.
- (84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).
- Published:
— with international search report
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: APPARATUS FOR DETECTING AND TREATING TUMORS USING LOCALIZED IMPEDANCE MEASUREMENT



(57) Abstract: An embodiment of the invention provides an apparatus (10) for detecting and treating tumors using localized impedance measurement. The apparatus comprises an elongated delivery device (12) that includes a lumen (13) and is maneuverable in tissue. An impedance sensor array (22a) is deployable from the elongated delivery device (12) and configured to be coupled to at least one of an electromagnetic energy source (20) or a switching device (29). The impedance array (22a) includes a plurality of resilient members (18mpl), at least one resilient member (18) of the plurality of resilient members (18mpl) being positionable in the elongated delivery device (12) in a compacted state and deployable with curvature into tissue from the elongated delivery device (12) in a deployed state. In the deployed state, the plurality of resilient members (18mpl) defines a sample volume (5sv). At least one resilient member (18) includes an impedance sensor (22) and at least a portion of the impedance array (22a) is configured to sample tissue impedance through a plurality of conductive pathways. An energy delivery device (18e) is coupled to one of the sensor array (22a), the at least one resilient member (18) or the elongated delivery device (12).



WO 02/32335 A1

**APPARATUS FOR DETECTING AND TREATING TUMORS USING
LOCALIZED IMPEDANCE MEASUREMENT**

5 **Field of the Invention**

 This invention relates generally to a method for performing tissue
characterization using minimally invasive methods. More particularly, the
invention relates to a method and apparatus for performing an in vivo tissue
characterization to identify and discriminate between diseased and healthy tissue
10 using localized measurement of tissue impedance. Still more particularly, the
invention to relates to method and apparatus for performing tissue
characterization before during and after ablative therapy using localized complex
impedance measurement to monitor and titrate the delivery of ablative therapy to
improve clinical outcomes.

15

BACKGROUND OF THE INVENTION

 Various ablative therapies such as radio-frequency, microwave and laser
ablation can be used to treat benign and cancerous tumors. In theory, such
methods are intended to produce physiological and structural changes to cause
20 cell necrosis or destruction of the selected target tissue. However in practice,
there are numerous difficulties in the use of ablative procedures to treat
cancerous tissue, these include (i) locating the target tissue, (ii) identifying or
biopsying the disease state of the tumorous tissue (iii) distinguishing between
diseased tissue versus healthy tissue, (iii) placing and maintaining the position of
25 the ablation apparatus within the target tissue site, (iv) monitoring the progress
of ablation including the developing ablation volume, (v) minimizing injury to
adjacent critical structures (vi) assuring complete ablation of the tumor mass
including assurance of a sufficient healthy tissue margin and (vii) assessing
degree of the completed ablation. Current ablative therapies have not
30 considered nor provided solutions to these problems. Thus, there is a need for

an apparatus and method to address these difficulties and other unmet needs in performing ablative therapies for the treatment of cancer, tumors and other diseases.

5

SUMMARY OF THE INVENTION

An embodiment of the invention provides an apparatus for detecting and treating tumors using localized impedance measurement. The apparatus comprises an elongated delivery device that includes a lumen and is maneuverable in tissue. An impedance sensor array is deployable from the elongated delivery device and configured to be coupled to at least one of an electromagnetic energy source or a switching device. The impedance array includes a plurality of resilient members, at least one of the plurality of resilient members being positionable in the elongated delivery device in a compacted state and deployable with curvature into tissue from the elongated delivery device in a deployed state. In the deployed state, the plurality of resilient members defines a sample volume. At least one of the plurality of resilient members includes an impedance sensor and at least a portion of the impedance array is configured to sample tissue impedance through a plurality of conductive pathways. An energy delivery device is coupled to one of the sensor array, the at least one resilient member or the elongated delivery device.

The apparatus can be configured to detect, locate and identify tumorous tissue at a selected tissue site using impedance measurements such as multi-pathway measured impedance, complex impedance and impedance vector measurements. For complex impedance real and imaginary components of the impedance signal can be used to determine more refined bioelectric parameters such as interstitial and intracellular impedance and cell membrane capacitance that provide greater sensitivity and predictive power of cell necrosis or malignancy. Also, the apparatus can also be configured to utilize one or more impedance measurements to monitor a target tissue site and control the course of ablative therapy before during or after the delivery of ablative energy or other treatment to the tissue site. Accordingly the apparatus can be configured to be

used independently or in conjunction with another ablative apparatus such as an RF, microwave or laser ablation apparatus. Further, the apparatus can be configured to utilize multi-path impedance measurement to monitor two or more tissue volumes including a tumor volume, a developing ablation volume and an adjacent anatomical structure. Additional embodiments of the apparatus can also be configured to utilize impedance measurements such as complex, vector or locus impedance measurements to generate an image of a target tissue site and display the image to facilitate the location and monitoring of a tumor and/or ablation volume.

In the use, the apparatus would be positioned at selected tissue site previously imaged and found to contain a tumor or other tissue mass. The apparatus would be introduced and positioned at the tissue site using the elongated delivery device or an introducing device known in the art. The impedance array would then be deployed and used to measure impedance including complex impedance and capacitance through one or more conductive pathways. This information could be analyzed by coupled logic resources and then utilized to locate the position of and borders of the tumor volume and/or identify the tumor or tissue type. Also the information could be processed by the logic resources or other processing means to generate an image of the tissue site including the tumor volume which could utilize the locus of impedance as a way to indicate the center of the tumor mass or otherwise visually enhance the detection and display of the tumor mass. This information could then be used to position the energy delivery to produce the desired ablation volume. Once the energy delivery device was positioned, the impedance array could then be utilized to monitor and/or control the delivery of ablative energy or therapy to the tumor volume including monitoring the size and shape of a developing ablation volume in relation to size and location of the tumor volume. This allows the medical practitioner to not only determine the degree to which the tumor volume has been ablated, but also allows for the control of the amount of healthy tissue margin around the tumor volume one or all of which allow for the determination of a desired clinical endpoint. Further, it allows the practitioner to

titrate or otherwise control the delivery of energy or other ablative therapy to control rate of growth of the ablation volume (and in turn the overall ablation time) as well as the final shape and size of the tumor volume. Multiple tissue volumes can be simultaneously monitored and compared to monitor progress of

5 the ablation volume, assure uniform ablation or necrosis throughout the tumor or ablation volume and provide real time assurance that surrounding healthy tissues and structure were not injured. For example, tissue volume at the center, and one or more peripheries of the tumor mass could be simultaneously or near simultaneously monitored to assure uniform necrosis at all locations and hence

10 throughout the tumor volume. Impedance measurements can be simultaneously or sequentially at multiple conductive pathways passing through the target volume (at convergent divergent and paths) to provide a higher confidence of uniform ablation by reducing the size of un-sampled zones within the target volume as well any directional bias of the measurements. The multiple

15 conductive pathways can be selected electronically via a controllable switching device or manually by rotational, lateral or longitudinal movement of the impedance array within the target volume. In the former case, the user could program the conductive pathways via a coupled monitoring device and in the latter, the user could rotate, advance, retract or deflect the impedance array via

20 the elongated delivery device or via a deployment, advancement or deflection device mechanically coupled to the impedance array or delivery device. In addition to real time impedance measurement during the ablation process, measurements can also be taken post ablation at one or more pathways, (including pathways different than those used during inter-ablative monitoring)

25 and compared to baseline measurements or an impedance database to provide a further indication of a complete ablation and/or clinical endpoint. Endpoints can also be determined based on ratios of intracellular to interstitial impedance as well as a characteristic shape of the impedance or complex impedance curve including determinations of thresholds, slopes or inflection points.

Various aspects of the invention can also be directed to display impedance measurements in a variety of manners that are both user-friendly and easily discernible by the user/medical practitioner. In an embodiment, the loci of impedance of a sample volume or an impedance vector of the sample volume can be displayed as icons to facilitate tumor identification and positioning of an energy delivery or ablative device within the tumor mass. In related embodiments logic resource of the apparatus could be configured to use impedance vector measurements to determine the radial direction of the tumor from the impedance array or energy delivery device and display this information in the form of a directional or pointing icon.

BRIEF DESCRIPTION OF THE FIGURES

Figure 1 is a lateral view illustrating the placement at a tissue site of an embodiment of an apparatus for detecting and treating tumors using localized impedance measurement.

Figure 2 is a lateral view illustrating the elements of an apparatus for detecting and treating tumors using impedance measurement including an elongated delivery device, impedance sensor array, sensors, resilient members, energy delivery device and advancement member.

Figure 3a is a schematic view of an embodiment of the impedance sensor array configured to measure impedance of a tissue volume via a plurality of selectable conductive pathways.

Figure 3b is a schematic view illustrating of an embodiment of the impedance array illustrating the use of primary and secondary conductive pathways and conductive pathway angle.

Figures 4a-4c are perspective views illustrating various arrangements of the emitting and detecting members; Figure 4a illustrates an embodiment having a centrally positioned a return electrode surrounded by other impedance sensing members; Figure 4b illustrates an embodiment having the return electrode eccentrically positioned respect to other impedance sensing members; Figure 4c

illustrates an embodiment having multiple and independently positionable impedance sensor arrays.

5 Figure 5 is a perspective view illustrating the use of multiple groups of conductive pathways to sample multiple tissue volumes in an embodiment of the invention as well as determine impedance vectors and loci of impedance for each sample volume.

10 Figure 6 is a perspective view illustrating an embodiment of an apparatus for detecting and treating tumors including an impedance monitoring having memory resource and logic resources including software modules to analyze impedance data and generate impedance profiles and images.

Figure 7a is a plot of tissue impedance curve illustrating the frequency dependency of impedance.

Figure 7b is a plot of tissue complex impedance curves illustrating the frequency dependency of complex impedance.

15 Figures 8a-8d are plots of impedance curves illustrating the use of multiple frequency impedance curves to monitor the time course of an ablation.

Figures 8e-8g are plots of complex impedance curves (imaginary vs. real values) illustrating the use of complex impedance curves to monitor the time course of an ablation.

20 Figures 9a-9c are plots of complex impedance curves illustrating the use of complex impedance curves to identify tissue type or condition.

Figure 10 is a plot of spectral signal intensity verses time for a sample volume of ablating tissue illustrating quantitative determinants of an ablation endpoint.

25 Figure 11 is a perspective view illustrating a three-dimensional plot of complex impedance.

Figure 12a is a lateral view illustrating an embodiment of the introducer.

Figures 12b and 12c are cross sectional views illustrating cross-sectional profiles of the introducer.

30 Figure 13 is a lateral view illustrating an embodiment of a deflectable introducer along with the components of the introducer.

Figure 14 is a lateral view illustrating an embodiment of a tissue biopsy and treatment apparatus with a hand piece and coupled aspiration device, fluid delivery device and fluid reservoir.

5 Figures 15a-15f are lateral views illustrating various configurations of the electrode including ring-like, ball, hemispherical, cylindrical, conical and needle-like.

Figure 16 is lateral view illustrating an embodiment of a needle electrode configured to penetrate tissue.

10 Figure 17 is lateral view illustrating an embodiment of an electrode having at least one radius of curvature.

Figure 18 is lateral view illustrating an embodiment of the electrode having at least one radius of curvature, sensors and a coupled advancement device.

15 Figure 19 is a perspective view illustrating an embodiment of the electrode that includes insulation sleeves positioned at exterior surfaces of the resilient members or electrodes so as to define an impedance sensor length or an energy delivery surface.

20 Figure 20 is a perspective view illustrating an embodiment of the electrode that includes multiple insulation sleeves that circumferentially insulate selected sections of the electrode(s).

Figure 21 is a perspective view illustrating an embodiment of the electrode with insulation that extends along longitudinal sections of the electrodes to define adjacent longitudinal energy delivery surfaces.

25 Figure 22 is a cross-sectional view of the embodiment of Figure 21.

Figure 23 is a lateral view illustrating an embodiment of the apparatus with an electrode having a lumen and apertures configured for the delivery of fluid and the use of infused fluid to create an enhanced electrode.

30 Figure 24 is a perspective view illustrating an embodiment of an impedance-sensing member that includes a conductive coating that can be configured to produce an impedance gradient within the sensing member.

Figures 25a-25c are perspective views of an embodiment of an energy delivering ablation apparatus using frequency controlled positionable ablation fields.

5 Figures 26a –26c are plots of energy density or concentration versus lateral distance from the electrode /energy delivery device of the embodiment of Figures 25a-25c.

Figure 27 is a flow chart illustrating a method for generating and displaying impedance derived images.

10 Figure 28 is a block diagram illustrating a controller, power source, power circuits and other electronic components used with an embodiment of a control system other embodiments of the invention.

Figure 29 is a block diagram illustrating an analog amplifier, multiplexer and microprocessor used with an embodiment of a control system or other embodiments of the invention.

15 Figure 30 is a lateral view illustrating a control and display unit used in various embodiments of the invention.

Figure 31 is a plot showing an embodiment of an impedance measurement duty cycled signal super-imposable on an RF treatment signal under selectable threshold conditions

20

DETAILED DESCRIPTION

Embodiments of the present invention provide an apparatus and method for performing tissue characterization using localized impedance measurement including complex impedance measurement to locate and diagnose a tumor, accurately position an ablative apparatus, monitor the progress of an ablative treatment and determine clinical endpoints. Further these and other
25 embodiments of the invention can be configured to measure and analyze bioelectric parameters with enhanced predictive power of cell metabolism along with associated images that allow for real time control of the ablative process
30 awhile significantly reducing the risk of incomplete ablation or unwanted damage to critical anatomical structures. Each of the disclosed embodiments

may be considered individually or in combination with other variation and aspects of the invention. The method and apparatus provided herein are useful in treating cancerous tumors in organs and tissue throughout the body including but not limited to the liver, bone, breast, lung and brain. They are also useful and
5 equally applicable to treatment of benign tumors, growths and otherwise abnormal or enlarged tissue that requires removal, resection or modification by surgical or minimally invasive means.

Localized monitoring of impedance provided in various aspects of the invention is particularly beneficial for use in the treatment of tumors and
10 tumorous tissue by ablative therapies such as RF, microwave, laser and chemical ablation. These and related ablative therapies causes disruption of cell membranes resulting in impedance change in the interstitial fluid but only in the affected tissue with minimal or no changes to the surrounding tissue. Previous attempts to measure impedance using a full electrical circuit through the
15 patients body had the drawback of not being able to detect tissue localized impedance by failing to consider the problems involved including the following (i) the signal is too small in relation to and/or mask out by the impedance of the entire impedance measurement system including the conductive pathway through body the ground pad electrodes and associated wires; (ii) the
20 measurement was made too far away on the body from the desired tissue site and is thus again masked out; and (iii) the localized impedance was masked out by RF or other ablative energy signal delivered to the tissue. Embodiments of present invention provide solutions to these problems to detect localized impedance changes, particularly those changes occurring during an ablation
25 procedure through the use of impedance arrays positioned at the target tissue to measure impedance including complex impedance and other bioelectric properties described herein

A discussion will now be presented of impedance measurement theory and impedance measurement methods employed by embodiments of the
30 invention. In order to measure in tissue impedance or impedivity (which typically has units of impedance/cc of tissue at 20°C) a current is applied across

the tissue and the resulting voltages are measured. This current, known as the excitation current or excitation signal is relatively small in comparison to an ablative RF or other ablative current and hence results in no appreciable ablative effect. In various embodiments the excitation current can range from 0.01 ma
5 to 100 amps with specific embodiments of 0.1, 1.0 and 10 amps which can be delivered in a continuous or pulsed fashion using a duty cycle. In various embodiments, the duty cycle can be in the range of 5 to 50 % with a pulse duration of 10 to 200 ms. The average power delivered over the course of the duty can be in the range of 0.1 to 10 watts. In these and related embodiments
10 the excitation current source is used to measure voltage differences between two or more selected impedance sensors/sensing member in a bipolar mode or one or more sensors/sensor members and a common ground. The known excitation current and measured voltage are then used to derive impedance using algorithms and methods described herein and/or known in the art.

15 Because different frequencies conduct differently through different tissue types some tissue is more or less conductive at certain frequencies. Accordingly, depending upon the tissue type or condition to be detected, the sensing or excitation signal can be varied or otherwise controlled to improve one or more of the sensitivity, accuracy, precision and resolution of an
20 impedance measurement. In various embodiments the excitation signal can be a mono-frequency or a multi-frequency signal and can be constant or variable. In an embodiment, improved signal resolution and thus more precise tissue analysis and characterization can be achieved by use of a multi-frequency excitation signal and/or an excitation signal varied across a broad range of
25 frequencies. In various embodiments this range of frequencies can be from about 1 Hz to about 1 MHz with specific embodiments of 0.5Hz, 1, 5, 10, 25, 50, 100, 250, 500 and 750 kHz. Since the bioelectric distinctions (e.g. phase angle, impedance) between cancerous and healthy tissue can be the greatest at low frequencies such as 100 Hz, in exemplary embodiments measurements can
30 be taken over a plurality of excitation frequencies below 100 Hz, with specific embodiments of 3,4,10 and 20 frequencies below 100 Hz. Other embodiment

can be combine measurements below 100Hz with those between 100Hz to 5kHz.

Further embodiments of the invention can be configured to measure impedance at different excitation frequencies (either concurrently or sequentially), to obtain more robust data and hence more refined clinical diagnostic information. Using these and other data and methods a plot of impedance versus frequency can be generated for a sampled tissue volume and analyzed to determine tissue type and tissue conditions of the sample volume as is more fully described herein.

Complex impedance includes both real and imaginary components, which reflect the phase shift between voltage and current (e.g. the voltage can lead or lag current depending on the electrical properties of the tissue). Various embodiments of the invention can be configured to record and both the real and imaginary components of complex impedance. This provides the benefit of providing more comprehensive information on the tissue allowing analysis with a greater degree of accuracy, precision and resolution. These components can be determined by passing an excitation current through the target tissue and measuring impedance and/or any phase shift between the current and voltage as the signal is conducted through the target tissue.

In related embodiments, real and imaginary components of impedance can be used to determine intracellular impedance, interstitial impedance and cell membrane capacitance. These three elements alone or in combination can be used to uniquely characterize and identify tissue type and condition with increased amounts of specificity. In an embodiment, the monitoring device, or other logic resources can be configured to utilize one or more of these three parameters (the "three parameters") to characterize an amount of ablation or progression of tissue ablation from an ablative treatment such as RF ablation or ablative method described herein. The characterization can be done by a software module resident within the monitoring device, power supply or coupled logic resources all described herein.

In specific embodiments, the three parameters can be used to detect various physiologic indicators of ablation and cell necrosis including cell lysis, cell membrane swelling (indicated by an increase in membrane capacitance), cell membrane rupture (indicated by a sharp decrease in membrane capacitance), a decrease in extracellular fluid (indicated by an increase in intracellular impedance) and an increase in intracellular fluid (indicated by a decrease in extracellular fluid). Other parameters which can be calculated and used for detection and control purposes include the absolute value of the impedance or admittance, the phase of the impedance (e.g. the phase difference between the current and the voltage), the capacitance or a function of a combination of the impedance and admittance components.

Specific embodiments of the invention can be configured to detect and/or control for threshold increases or decreases in one or more of the three parameters (or other variables) including increases or decreases in the ranges of 1.1:1.0 to 100:1.0 with specific embodiments of 1.5:1.0, 2:1, 3:1, 4:1, 5:1, 10:1, 20:1 and 50:10. Related embodiments can be configured to detect and/or control for combinations of increases or decreases in the parameters including but not limited to a rise followed by a decrease in extracellular impedance, a decrease followed by an increase in intracellular impedance and an increase followed by a decrease in cell membrane capacitance. Other related embodiments can be configured to detect, monitor and control for changes in the slopes of the curves of one or more of the three parameters. Still other related embodiments can employ PID control methods known in the art utilizing combinations of proportional, integral or derivative changes in the three-parameter curves.

Embodiments of the invention can incorporate the three parameters into electronic algorithms/ software programs which are configured to do one or more of the following: (i) control the delivery of power to the target tissue site, (ii) provide the medical practitioner with prompts and diagnostic information about the course of the ablation/treatment process, and (iii) provide the medical practitioner with an indication of a clinical endpoint.

Referring now to the drawings, Figure 1 shows an embodiment of an impedance monitoring and treatment apparatus 10 configured to detect and treat a tumor mass 5'' in a target tissue site 5' by sampling the impedance of the tissue mass and delivering energy or other ablative treatment to produce an ablation volume 5av. The apparatus can be configured to measure impedance, including complex impedance, before during and after an ablation so as to perform tissue identification at the target site, monitor the progress of an ablation procedure including the developing ablation volume and quantitatively determine a clinical endpoint for the procedure.

Referring now to Figures 1 and 2, an embodiment of impedance treatment apparatus 10 comprises an elongated member or introducer 12 having a lumen 13, a proximal portion 14, a distal end 16, one or more resilient members 18 positionable in lumens 13 and one or more impedance sensors 22 disposed on members 18 or impedance sensing members 22m positionable in lumens 72 disposed within members 18. Distal end 16 may be sufficiently sharp to penetrate tissue including fibrous and/or encapsulated tumor masses, bone, cartilage and muscle. Lumens 13 may extend over all or a portion of the length of introducer 12. Members 18 can comprise a plurality 18pl of resilient members 18 configured to be positionable in lumen 13 and advanceable in and out of distal end 16 by an advancement device 15 or advancement member 34 or other means described herein. Resilient members 18 can be deployed with curvature from introducer 12 to collectively define a volume 5av in target tissue site 5'. In an embodiment all, or a portion, of one or more members 18 can be an energy delivery device or energy delivery member 18e described herein. Energy delivery device 18e can be coupled to an energy source or power supply 20 and can also include one or more lumens 72.

Embodiments of the invention can be adapted, integrated otherwise applicable to a number of ablative therapies including, but not limited to, radio-frequency (RF) ablation, cryo-ablation, brachytherapy, alcohol tissue ablation, chemical ablation, microwave ablation, laser ablation, thermal ablation, electroporation ablation, conformal beam radiation ablation, standard radiation

ablation, high intensity focused ultrasound ablation, photo-dynamic therapy ablation. These and related embodiments can comprise an energy delivery device and sensing device coupled to a power supply.

For ease of discussion, the energy delivery and sensing apparatus will be an RF based apparatus and power supply 20 will be a RF power supply; however, all other embodiments discussed herein are equally applicable. In and embodiment the RF power supply can be an RF generator configured to deliver a treatment current 20t for tissue ablation while simultaneously or near simultaneously (using a multiplexing/switching device) delivering a low power sensing or excitation signals 20e across at one or more frequencies for making complex impedance measurements and subsequent analysis of the target tissue. The excitation signal 20e can be delivered across a broad band of frequencies in the range of 1 to 1 MHz. In various embodiments, the excitation signal is delivered at a lower frequency then the treatment signal (typically 460 +/- 60 kHz). In an embodiment, the excitation signal is less than 400 kHz. In other embodiments, the sensing signal is in the range of 1 h to 100 kHz, with specific embodiments of 0.25, 0.5, 1, 5, 10, 25, 50 and 75 kHz. In alternative embodiments, the excitation signal is delivered at frequencies above the treatment frequency and thus can be greater than 520kHz. Further the frequency and power differences between the excitation and treatment signals 20e and 20t can be monitored and set point controlled using circuitry and control algorithms known in the art. Also the frequency and power difference between the two signals can varied responsive to one or more electrical parameters to maximize the accuracy and precision of impedance measurements and reduce interference (e.g. bleed over) from the treatment signal 20t. These electrical parameters include but are not limited to impedance, treatment current, treatment frequency, excitation current and excitation frequency.

In various embodiments, introducer 12 can be flexible, articulated and steerable and can contain fiber optics (both illumination and imaging fibers), fluid and gas paths, and sensor and electronic cabling. In an embodiment introducer 12 can be configured to both pierce tissue and also be maneuverable

within tissue. This can be achieved through the use of flexible portions coupled to a tissue piercing distal end 16 that can be a needle or trocar tip integral or joined to introducer 12. Introducer 12 can be sufficiently flexible to move in any desired direction through tissue to a desired tissue site 5'. In related
5 embodiments, introducer 12 is sufficiently flexible to reverse its direction of travel and move in direction back upon itself. This can be achieved through the use of flexible materials and/or deflecting mechanisms described herein. Also, introducer 12 can be coupled at its proximal end 14 to a handle 24 or handpiece 24. Handpiece 24 can be detachable and can include ports 24' and actuators
10 24".

One or more impedance sensors 22 can be coupled to introducer 12, resilient members 18 or energy delivery device 18e. In an embodiment, sensors 22 can comprise one or more sensing members 22m that can be positionable within lumens 72 of members 18 and configured to be advanceable
15 in and out of individual members 18 or can be coupled to an exterior of resilient member 18. Sensing members 22m can comprise a plurality of members 22mpl positioned in multiple resilient members 18. Also apparatus 10 can also have impedance sensors 22 disposed along elongated member 12 and other locations outside of the target tissue site for measurement and determination of
20 the total impedance across the full electrical circuit between the terminals of power supply 20 (i.e. through the patient's body and into the ground pad). The total impedance can be monitored and otherwise utilized to improve the accuracy and precision of the localized impedance measurement from the target site.

Impedance sensing members 22m, or sensors 22 coupled to resilient
25 members 18 can be deployed independently or simultaneously to enable probing of target tissue 5' in multiple locations so as to measure impedance in multiple locations and/or through multiple conductive pathways 22cp. Deployment of impedance sensing member 22m or sensors 22 can be controlled such that
30 telemetry can be used with impedance feedback to identify tissue types and map the topography of tissue masses, tumors or tissue structures.

Impedance sensing members 22m can also be deployed with curvature from members 18 to collectively define a volume 5sv (also called sample volume 5sv) that is volumetrically sampled by sensing member plurality 22mpl. Collectively, the plurality 22mpl of deployed impedance sensor members 22m or
5 plurality 18pl of deployed resilient members 18 with coupled impedance sensors 22 can comprise a three-dimensional or volumetric impedance sensor array 22a. By having sensors 22 in multiple locations and planes sensor array 22a is configured to volumetrically sample (e.g. sample in multiple locations and through multiple conductive pathways) tissue within target tissue site 5' including tumor mass 5". Sensor array 22a is further configured to be able to
10 simultaneously sample tissue at multiple locations within volume 5sv or tissue site 5' to perform one or more of the following: (i) locate the position of the tumor mass 5", (ii) discern the position or deployment distance of the energy delivery devices 18, (iii) monitor the developing ablation volume, (iv) perform
15 tissue sensing identification by comparing signals between two or more sites (e.g. known healthy tissue and suspected diseased tissue). In various embodiments sensor array 22a and/or member plurality 18pl can be configured to define a variety of shapes for sample volumes 5sv including, but not limited to, a hemisphere, a sphere, an oval, a cone, pyramidal, a polyhedron or a
20 tetrahedron.

Each resilient member 18 can have one or more impedance sensing members 22m and/or sensors 22 that can be arranged in a variety of configurations to perform one or more desired functions described herein (e.g. tissue identification, ablative monitoring etc.). Referring now to Figure 3a,
25 sensing members 22m can be configured to measure impedance in either bipolar between two or more members 22m or a mono-polar mode between one or more selected members 22 and a common ground such as a ground electrode 22g or ground pad electrode 22gp. Switching between the two modes can be controlled by logic resources and/or a switching or device 29 coupled to or
30 integral with an impedance monitoring device 19 or power supply 20. Further switching device 29 can be configured to allow the user to define and select one

or more conductive pathways 22cp to measure impedance. In use, these and related embodiments allow the user to select any number of conductive pathways and in a pattern 22pp that circumscribe or otherwise defines a sample volume 5sv of interest. Also the use of switching device 29 in these
5 embodiments allows the user to measure impedance simultaneously or sequentially through the selected pathways. Further switching device 29 and/or apparatus 10 can be so configured to allow the user to dynamically change or switch between pathways to do one or more of the following: (i) change the number of pathways through a selected sample volume allowing increased
10 signal resolution and statistical confidence of predicted tissue conditions; (ii) change the angle between two or more conductive pathways; (iii) change the size of the sample volume (iv); switch between a first and second sample volume; and (v) compare two or sample volumes simultaneously.

 In an embodiment shown in Figure 3b, conductive pathways 22cp can
15 include a primary pathway(s) 22cp' and an alternative pathway(s) 22cp". The alternative pathway can be at a selectable angle 22cpa from the primary pathway and can share points in common with the primary pathway. Suitable angles include the range of 1 to 360° with particular embodiments of 30, 45, 90 and 270° from a lateral axis 22la of the primary pathway. Alternatively, the
20 alternative conductive pathway can share one or more points in common with the original pathway or be parallel with the original pathway but offset a selectable lateral distance 22ld. Also repetitive scans of impedance including sweep scans and sequential sweep scans (e.g. sequentially sampling from one side of a sample volume to the other, similar to radar) can be made through one
25 or more selected conductive pathway of a selected sample volume to monitor the time course of ablation as well obtain improved signal to noise ratios and signal resolution for image analysis.

 Changing the angle and/or lateral offset of the conductive pathway used to measure impedance can be accomplished through a variety of means
30 including but not limited to: (i) selectively switching impedance sensors 22 or sensing elements 22m off and on (ii) selectively switching sensing elements 22

from a monopolar mode to a bipolar mode and visa versa, (for RF
embodiments) using switching device 29 (iii) configuring the probe array to be
rotatable and/or deflectable, and (iv) the use and/or deployment of a second
array either on the same or different device. Switching can be accomplished
5 through the use of a switching or multiplexing device 29 which can be
programmable or controlled by logic resources 191r described herein.

In one embodiment the data from alternative conductive pathways or
group of pathways can be integrated with measurements from the primary
conductive pathways for analysis and imaging purpose or in an alternative
10 embodiment can be analyzed and displayed separately allowing for a
comparison of both measurement and image from the primary and alternative
group of pathways. The benefit of the former is a more representative and
uniform sample of impedance and the later the ability to detect for uniformities
of impedance within the sample volume.

15 In use, such embodiments allow the medical practitioner to sample or
image a larger tissue volume than single pathway sampling, sample multiple
tissue volumes including simultaneous sampling without having to reposition
the apparatus or impedance array. This capability reduces procedure time
generally enhances the usability of the apparatus. Further, such embodiments
20 also provide a more accurate and representative signal of the target tissue
volume by selecting conductive pathways to control the shape and size of the
sample volume to sample only the area of interest eliminating any potential
masking or undesired impedance contribution from surrounding non-target
tissue. Also the ability to switch the angle of the pathway eliminates or reduces
25 any directional bias in the impedance measurements. Finally, by virtue of
having a larger and volume distributed sample size for a given volume of tissue,
the use of multiple conductive pathway impedance measurements provides a
more representative measurement of impedance for the selected volume
improving the accuracy and precision of the impedance measurement as well as
30 improving signal and image resolution in one or all three dimensions.

Referring now to Figures 4a–4c in various embodiments, impedance sensing members 22m can be arranged in arrays 22a having a variety of geometric arrangements and relationships so as to electrically sample different volumes of tissue 5sv using different conductive pathways 22cp. Such
5 embodiments provide the benefit of improved acquisition, accuracy and analysis of the impedance signal 19p from a given sample volume 5sv to compensate for signal hysteresis, noise (due to energy delivery etc.,) directional bias or other error. They also provide the benefit of simultaneous sampling and comparison of two or more tissue volumes to perform tissue identifications.

10 Referring now to Figures 4a–4c, conductive pathways 22cp can have a variety of configuration and orientations all selectable by the user. In an embodiment the conductive pathways 22cp can be evenly distributed or spaced within the sample volume 5sv. This can be achieved by either the configuration of the members 22m, through the use of switching device 29 or a combination
15 of both. Alternatively, the conductive pathways can be aligned with respect to one or more sensing members 22m, the introducer or the tumor volume 5" itself. In an embodiment shown in Figure 4a, one member 22mc can be positioned at the center of tissue volume 5sv with other members 22m positioned in a surrounding relationship so excitation current travels in a
20 plurality 22pp of conductive pathways 22cp to and from the center of the sample volume 5sv to the outlying impedance sensor members 22m. In use, this configuration results in an impedance measurement for the sample volume 5sv which is an average of the individual impedance for each conductive
25 pathway providing the benefit of a more a statistically representative sample of impedance for a selected tissue volume than provided by a single pathway alone. Members 22m can be collectively coupled to a positive terminal of power supply 20 with member 22mc configured as a return electrode and coupled to a return terminal of power supply 20.

30 In a related embodiment shown in Figure 4b, member 22mc can be eccentrically positioned with respect to members 22m and/or positioned on the periphery of a sample volume defined by members 22m. Again this

embodiment provides benefit of an average and thus more representative impedance measurement for the sample volume. However, this configuration also provides the benefit of being able to more readily detect and locate non-uniformities 5nu in impedance and hence tissue properties occurring on the boundaries or otherwise non centered portions of the tissue volume. Use of switching device 29 allows for the dynamic switching of any of the sensing members 22m to a return electrode 22mc to more readily detect the location of a potential non-uniformity within the sample volume by rapidly scanning different portions of the periphery of the volume.

Alternatively as shown Figure 4c, members 22m can comprise a first array 22a1 (such as perpendicular array) and a second array 22a2. First array 22a1 can be rotated to obtain different conductive paths to second array 22a2 so as to sample different tissue volumes and/or provide multiple samplings of the same volume (via different conductive paths) to improve accuracy and precision of the measurement and reduce noise. In use this embodiment also allows detection of incomplete ablation by comparing a measured impedance from a first group of conductive pathways 22cp1 defined by first array 22a1 to a second group of conductive pathways 22cp2 defined by second array 22a2.

In various embodiments apparatus 10 can be configured to simultaneously sample different locations within target tissue site 5' utilizing switching device or multiplexer 29 or other switching means described herein or known in the art. In an embodiment shown in Figure 5 a first group of selected conductive pathways 22cp' can be used to sample a local first volume 5sv1 and a second group of selected conductive pathways 22cp'' can be selected to do so for a second volume 5sv2 and a third group of selected conductive pathways 22cp'; can be so selected to do so for a larger or global sample volume 5sv3 defined or circumscribed by multiple sensor tipped members 18 or sensing members 22m. Each sample volume results in a separate impedance profile 19p. Thus sample volumes 5sv1, 5sv2 and 5sv3 produce impedance profiles 19p1, 19p2 and 19p3 respectively, all or portion of which can be compared to one another or a database of impedance profiles 19db using comparison/pattern recognition

algorithms of module 19m other software or computational means. In a related embodiment the measured impedance signal for each sample volume can be integrated or otherwise analyzed by module 19m or other computational means to determine an impedance vector 22v and loci of impedance 22i for each
5 respective sample volume (e.g. impedance vectors 22v1, 22v2, 22v3; and impedance loci 22i1, 22i2 and 22i3).

Referring now to Figure 6, in an embodiment one or more impedance sensors 22 or sensing members 22m of can be coupled to an impedance measurement and monitoring device 19. Monitoring device 19 includes
10 circuitry described herein to measure voltage from the excitation current and subsequently calculate impedance. Further monitoring device 19 can also be configured to measure, calculate and record complex impedance, an impedance profile 19p and a complex impedance profile 19pc resulting from various tissue bioelectric properties including, impedance conductance, capacitance etc. In an
15 embodiment monitoring device 19 can include logic resources 19lr such as a microprocessor and memory resources 19mr such as RAM or DRAM chip configured to analyze, store and display tissue impedance profile 19p and/or other bio-electric information derived from sensing member 22m and/or sensing array 22a. Impedance monitoring device 19 can also be coupled to a display
20 device 21 so as to display real time or stored impedance profiles images and other data generated by impedance monitoring device 19. Examples of display devices 21 include cathode ray tubes (CRTs), liquid crystal displays, plasma displays, flat panel displays and the like. Display device 21 can also be incorporated in an external computer coupled to impedance monitoring device
25 19.

In various embodiments, impedance monitoring device 19 or power supply 20 can be equipped with a number of features including but not limited to the following: (i) memory resources containing a database of characteristic impedance profiles (ii) a readout window for the impedance based diagnosis of
30 tissue type and/or condition, (iii) artificial intelligence algorithms/programming enabling the generator to learn from newly acquired impedance scans, (iv)

ability for the user to enter and teach the generator the correct tissue type and condition based on biopsy or pathology data, (v) ability to sense impedance on multiple frequencies simultaneously to improve speed, accuracy, and reduce effects of interference, (vi) ability to work with non-invasive pads (like electro-physiology pads) for measurement of complex impedance and performing targeted tissue assessment non-invasively, (vii) ability to monitor a reference signal and/or basic patient electro-physiological conditions for baseline comparisons with impedance readings and as additional information for the user; and (viii) programming to utilize the reference signal or signal to account for hysteresis, signal noise, cross talk and other signal interference using digital subtraction, suppression and other signal processing methods known in the art and thus improve a signal to noise ratio, signal sensitivity or resolution.

In various embodiments, apparatus 10 along with impedance monitoring device 19 can be configured to perform tissue identification, differentiation, ablation monitoring and mapping of tissue masses and structures. In specific embodiments, monitoring device 19 is configured to perform a tissue identification function using impedance information derived from sensors 22, sensing members 22m or array 22a. A discussion will now be presented on the background of tissue monitoring and identification using impedance measurement. Owing to variations in composition and morphology various tissue types have different electrical properties (e.g. conductance, inductance, capacitance etc) and therefore conduct electrical energy differently particularly at certain frequencies. For example cancerous tissue will typically have a significantly higher phase than the health tissue, particularly at low frequencies. These difference in electrical properties, particular conductance result, in a characteristic impedance profile 19p for a given tissue type or condition when the tissue is exposed to an excitation current at one or more specific frequencies. Impedance profile 19p can have one or more peaks 19pk, curves and other shapes that serve as a fingerprint of the tissue type or tissue condition. Accordingly by analyzing the impedance profile 19p and matching peaks, curve shapes, thresholds etc, profile 19p can be utilized by embodiments of the

invention to identify tissue types and conditions such as malignancy, vascularity, necrosis, thermal injury etc. Related conditions that can also be identified using this approach include abnormally mutated tissue, abnormally dividing tissue or hypoxic tissue

5 Further, many tissue types including cancerous tissue such as metastatic tissue, will have a signature profile 19p that can be readily identified and matched to a database of profiles using pattern recognition techniques or algorithms known in the art. Accordingly, apparatus 10 can include electronic algorithms or software modules 19m resident in logic resources 19lr of
10 monitoring device 19 or microprocessor 339 that are configured to analyze an impedance profile 19p including real and imaginary components and perform tissue identification and/or tissue differentiation between one or more sampled volumes 5sv. Modules 19m can include pattern recognition algorithms, curve fitting, fuzzy logic or other numerical methods known in the art. Also in an
15 embodiment, modules 19m can be configured to compare profile 19p to a database of profiles 19db stored in memory resources 19mr and use curve fitting or other numerical methods known in the art to provide and display a correlation coefficient or statistic (e.g. p value) indicative of the probability of a match to a given tissue type or condition. Module 19m can also include an
20 imaging sub-module 19mi, described herein, to generate and display an impedance image 4'.

In various embodiments the impedance and other bioelectric properties that can be analyzed to determine a tissue type or condition include complex impedance (real and imaginary components), extracellular impedance,
25 intracellular impedance, interstitial impedance, cell membrane capacitance, intracellular capacitance. In an embodiment, monitoring device 19 can be configured to analyze only selected frequencies of an impedance profile or other bioelectric property measurement that are known to identify or correlate to selected tissue characteristics, rather than analyzing the full frequency spectrum
30 of the profile. Such frequencies can be selected from a pre-existing database or determined in vivo using swept frequency methods described herein. This

approach presents the advantage of faster signal processing times, allowing a faster tissue assessment and diagnosis using fewer computational resources. In turn this enables the size, power requirements and complexity of the control and display instrumentation to be reduced

5 Referring now to Figure 7-10, in related embodiments apparatus 10 and monitoring device 19 can be configured to utilize complex impedance curves to identify and characterize different tissue types and conditions. Accordingly monitoring device 19 can be configured to measure generate and display curves or profiles 19pc of complex impedance. Curves 19pc can be both two-
10 dimensional and three-dimensional. For two-dimensional plots the x-axis can be the real component and the y-axis the imaginary component while three-dimensional plots can include an axis for time or frequency. This can be accomplished via algorithms within modules 19m or 19mi that receive input from impedance array 22a, perform complex impedance calculations known in
15 the art and curve fitting or transform functions described herein and subsequently output an impedance profile 19pc that is displayed on display device 21. As shown in Figure 7a and 7b, because tissue conducts differently at frequencies, measurements made across a range of excitation frequencies results in an impedance frequency response curve 19pf (Figure 7a) or a series of
20 complex impedance frequency response curves 19pcf (Figure 7b). Using either of the frequency response curves from Figures 7a or 7b, a particular frequency can be selected for subsequent impedance complex impedance measurements and analysis which has the greatest sensitivity for a given tissue type or condition and/or results in a complex impedance curve having the greatest
25 predictive value for the desired tissue type or condition. The selection can done using methods described herein or by calibration against a set of in vitro standards representative of the desired tissue condition, by visual determination/estimation of the user or a combination of both.

30 As shown in Figures 8a-8c, in an embodiment, the course of an ablation can be monitored using impedance measurements made at multiple frequencies. The impedance at some frequencies will rise, fall or do both over the time

course of the ablation. By combining impedance data from multiple curves the overall predictive value of the measurements for an ablation event or endpoint is greatly increased. Accordingly, using differential diagnosis methodology an ablation monitoring algorithm or module 19m can be configured to look for impedance characteristic curve shapes, slopes threshold etc in two or more impedance curves made at different frequencies as a predictor of an ablation endpoint. Such information can be used to provide a more reliable indicator of clinical endpoint as well monitor and titrate the delivery of ablative energy or ablative therapy to the requirements. Similarly, as shown in Figure 8d, differences in the impedance-frequency spectrum, pre, inter and post ablation can also be also be used to monitor and evaluate the ablation process.

In related embodiments shown in 8e-8g, complex impedance curves 19pc can be used to monitor and assess the ablation process including determination of clinical endpoints as described herein. Further as shown in Figures 9a-9c, the apparatus can be configured to utilize complex impedance curves to identify and characterize different tissue types, tumors etc. Related embodiments can be configured to generate and display three-dimensional plots of complex impedance utilizing time and or position as the third axis. For positional 3-D plots the locus of impedance 5li can be calculated and graphically displayed as is shown in Figure 10 or in 2-D as shown in Figure 5 or another graphical format known in the arts. Also impedance locus 5li can be utilized to characterize the ablation process and can be used to perform vector analysis of RF or microwave current or other ablative energy vector, (e.g. the magnitude and direction of the ablative energy), as well as vector analysis of physiologic indicators of cell necrosis, such as changes in interstitial conductivity. In various embodiments, the impedance locus 5li can utilized to facilitate location and display of tumor volume 5', ablation volume 5" or other desired tissue mass or volume at the target tissue site. The generation and display of the impedance locus 5li (in 2-D or 3-D) can be configured to provide the medical practitioner an easily discernable visual cue as to the location, size or movement of the ablation, tumor or other selected tissue volume.

In addition to identifying tissue types, monitoring device 19 along with impedance sensing arrays 22a can also be employed to monitor in real time the progression of an ablative procedure including the progression of an ablation volume 5av resulting from the delivery of energy to target tissue volume 5.

5 This reduces damage to tissue surrounding the targeted mass to be ablated. By monitoring the impedance at various points within and outside of the interior of tissue site 5', a determination of the selected tissue mass periphery can be made, as well as a determination of when cell necrosis is complete. If at any time sensor 22 determines that an impedance level or ablation endpoint has been met
10 or exceeded, then an appropriate feedback signal is inputted to power source 20 which then stops or otherwise adjust the levels of ablative energy delivered to electrodes 18 and 18'. The target tissue site 5'' can also be probed and interrogated by sensor array 22a after the completion of ablation to confirm that ablation is complete for the entire desired volume ablation volume. By probing
15 the ablated region with sensor array 22, the three-dimensional volume of the ablation can be assessed and the margin 5m of ablated healthy tissue beyond the tumor mass 5'' can also be measured.

Referring now to Figures 10, in embodiment for monitoring the ablative process the impedance signal intensity 19si for a sample volume of tissue
20 bounded by two or sensing members 22m or array 22a can be monitored over time using monitoring device 19, supply 20 or other bioelectric signal monitoring means known in the art. An endpoint for ablation can be determined based on either a selectable threshold value 19ts of signal 19si or an inflection point or change in slope 19ds (e.g. a derivative) of curve 19p or a combination
25 of both. In an embodiment signal 19p can comprise the subtraction of a baseline (or reference) impedance measurement 19sbl of a nearby, but non-ablated tissue volume, from a real time measurement 19srt of the target tissue volume during the time course of ablation. This compensates for any signal or tissue hysteresis over time. Values for 19ts and 19s can be input and stored in
30 logic resource 19lr coupled to impedance monitoring 19 or incorporated into an

electronic algorithm controlling the delivery of energy which can be stored in a controller or processor 338 coupled to power supply 20.

Turning now to a further discussion of introducer 12, in various embodiments, introducer 12 can be a trocar, catheter, multi-lumen catheter, or a wire-reinforced or metal-braided polymer shaft, a port device, a subcutaneous port device or other medical introducing device known to those skilled in the art. In various embodiments, introducer 12 as well as resilient member 18 can be configured to have varying mechanical properties along their respective lengths including, but not limited to variable stiffness, torquability, column strength, flexural modulus, pushability, trackability and other mechanical performance parameters known in the catheter arts. Referring to Figure 12a, this can be achieved through the use of stiff shafts sections 12''' disposed within portions of introducer 12 along its length 12''. It can also be accomplished through the use of braids, varying/tapered diameters and different materials (e.g. stiffer materials joined to flexible materials) positioned over portions of introducer 12. Sections 12''' made from different materials can be joined using introducer bonding methods known in the art such as hot melt junctions (with and without capture tubes/collates), adhesive joints, but joints and the like. The joining method can be controlled/selected so as to control the mechanical transition 12mt between two sections to a desired gradient (e.g. smooth vs. abrupt). In related embodiments, introducer 12 and/or member 18 can be configured to have stiffer proximal portions and more flexible distal portions so as to facilitate one or more of the following (i) introducer steerability and positioning of distal tip 16 at a selectable target tissue site 5', (ii) reduced risk of perforation, abrasion and other trauma during the positioning the introducer to the tissue site. In various embodiments, the transition from the stiffer to the more flexible portion can be configured to be either (i) gradual with a linear or curve-linear transition, (ii) a step or abrupt transition, and (iii) combinations thereof.

Referring to Figures 12b and 12c, introducer 12 can have a substantially circular, semicircular, oval or crescent shaped cross sectional profile 12cs, as well as combinations thereof along its length. Similarly, lumens 13 can have a

circular, semicircular, oval or crescent shaped cross section for all or a portion of the 12' length of introducer 12.

Suitable materials for introducer 12 and resilient member 18 include, but are not limited to, stainless steel, shape memory alloys such as nickel titanium alloys, polyesters, polyethylenes, polyurethanes, Pebax®, polyamides, nylons, copolymers thereof and other medical plastics known to those skilled in the art. All or portions of introducer 12 can be coated with a lubricious coating or film 12' which reduces the friction (and hence trauma) of introducer 12 with hepatic, pulmonary, bone and other tissue. Such coatings can include but are not limited to silicones, PTFE (including Teflon®) and other coatings known in the art. Also, all or portions of apparatus 10 including introducer 12 and members 18 can be constructed of materials known in the art that are optimized and/or compatible with radiation sterilizations (e.g. Gamma or E-beam). In related embodiments, all or portions of apparatus 10 can be configured (e.g. lumen diameter to length ratio, etc) to be sterilized by plasma (e.g. H₂O₂) sterilization by systems.

Referring now to Figure 13, in other embodiments all or portions of introducer 12 or resilient members 18 can be configured to be deflectable and/or steerable using deflection mechanisms 25 which can include pull wires 15, ratchets, cams, latch and lock mechanisms, piezoelectric materials and other deflection means known in the art. The amount of deflection of introducer 12 is selectable and can be configured to allow the maneuvering of introducer 12 through oblique turns in tissue, organs, organ ducts and blood vessels. In specific embodiments, the distal portions of introducer 12 can be configured to deflect 0-180° or more in up to three axes to allow the tip of introducer 12 to have retrograde positioning capability. Deflection mechanism 25 can be coupled to or integral with a moveable or slidable actuator 24'', 25' on handpiece 24. Mechanism 25 and coupled actuator 25' are configured to allow the physician to selectively control the amount of deflection 25 of distal tip 16 or other portion of introducer 12. Actuator 25' can be configured to both rotate and deflect distal tip 16 by a combination of rotation and longitudinal movement of the actuator.

Referring now to Figure 14, in various embodiments introducer 12 can be coupled at its proximal end 14 to a handle 24 or handpiece 24. Handpiece 24 can be detachable and can include ports 24' and actuators 24". Ports 24' can be coupled to one or more lumens 13 (and in turn lumens 72) and can include fluid and gas ports/connectors and electrical, optical connectors. In various embodiments, ports 24' can be configured for aspiration (including the aspiration of tissue), and the delivery of cooling, electrolytic, irrigation, polymer and other fluids (both liquid and gas) described herein. Ports 24' can include but are not limited to luer fittings, valves (one-way, two-way), toughy-bourst connectors, swage fittings and other adaptors and medical fittings known in the art. Ports 24' can also include lemo-connectors, computer connectors (serial, parallel, DIN, etc) micro connectors and other electrical varieties well known to those skilled in the art. Further, ports 24' can include opto-electronic connections which allow optical and electronic coupling of optical fibers and/or viewing scopes to illuminating sources, eye pieces, video monitors and the like. Actuators 24" can include rocker switches, pivot bars, buttons, knobs, ratchets, levers, slides and other mechanical actuators known in the art, all or portion of which can be indexed. These actuators can be configured to be mechanically, electro-mechanically, or optically coupled to pull wires, deflection mechanisms and the like allowing selective control and steering of introducer 12. Handpiece 24 can be coupled to tissue aspiration/collection devices 26, fluid delivery devices 28 (e.g. infusion pumps) fluid reservoirs (cooling, electrolytic, irrigation etc) 30 or power source 20 through the use of ports 24'. Tissue aspiration/collection devices 26 can include syringes, vacuum sources coupled to a filter or collection chamber/bag. Fluid delivery device 28 can include medical infusion pumps, Harvard pumps, syringes and the like. In specific embodiments, aspiration device 26 can be configured for performing thoracentesis.

Turning now to a discussion of resilient members 18 and sensing members 22, these members can be of different sizes, shapes and configurations with various mechanical properties selected for the particular tissue site. In one embodiment, members 18 can be needles, with sizes in the range of 28 to 12

gauge with specific embodiments of 14, 16 and 18 gauges. Resilient members 18 are configured to be in non-deployed positions while retained in introducer 12. In the non-deployed positions, resilient members 18 may be in a compacted state, spring loaded and generally confined within introducer 12 or substantially straight if made of a suitable memory metal such as nitinol. As resilient members 18 are advanced out of introducer 12 they become distended to a deployed state as a result of their spring or shape memory that collectively defines an ablative volume 5av, from which tissue is ablated as illustrated more fully in Figures 1 and 2. The selectable deployment of resilient members 18 can be achieved through one or more of the following approaches (i) the amount of advancement of resilient members 18 from introducer 12; (ii) independent advancement of resilient members 18 from introducer 12; (iii) the lengths and/or sizes of energy delivery surfaces of electrodes 18 and 18'; (iv) variation in materials used for electrode 18; (v) selection of the amount of spring loading or shape memory of electrode 18; and (vi) variation of the geometric configuration of electrode 18 in their deployed states.

As described herein, in various embodiments all or a portion of resilient member 18 can be an energy delivery device or member 18e. Turning to a discussion of energy delivery device and power sources, the specific energy delivery devices 18e and power sources 20 that can be employed in one or more embodiments of the invention include but are not limited to, the following: (i) a microwave power source coupled to a microwave antenna providing microwave energy in the frequency range from about 915 MHz to about 2.45 GHz (ii) a radio-frequency (RF) power source coupled to an RF electrode, (iii) a coherent light source coupled to an optical fiber or light pipe, (iv) an incoherent light source coupled to an optical fiber, (v) a heated fluid coupled to a catheter with a closed or at least partially open lumen configured to receive the heated fluid, (vi) a cooled fluid coupled to a catheter with a closed or at least partially open lumen configured to receive the cooled fluid (viii) a cryogenic fluid, (ix) a resistive heating source coupled to a conductive wire, (x) an ultrasound power source coupled to an ultrasound emitter, wherein the ultrasound power source produces

ultrasound energy in the range of about 300 KHZ to about 3 GHz, (xi) and combinations thereof. For ease of discussion for the remainder of this application, the energy delivery device 18e is one or more RF electrodes 18e and the power source utilized is an RF power supply. For these and related
5 embodiments, RF power 20 supply can be configured to deliver 5 to 200 watts, preferably 5 to 100, and still more preferably 5 to 50 watts of electromagnetic energy is to the electrodes of energy delivery device 18 without impeding out. The electrodes 18e are electro magnetically coupled to energy source 20. The coupling can be direct from energy source 20 to each electrode 18e respectively,
10 or indirect by using a collet, sleeve and the like which couples one or more electrodes to energy source 20.

 In various embodiments, electrodes 18e including impedance sensors 22 and sensing members 22m can have a variety of shapes and geometries. Referring now to Figures 15a-15f, example shapes and geometries can include,
15 but are not limited to, ring-like, ball, hemispherical, cylindrical, conical, needle-like and combinations thereof. Referring to Figure 16, in an embodiment electrode 18e can be a needle with sufficient sharpness to penetrate tissue including fibrous tissue including, encapsulated tumors cartilage and bone. The distal end 18de of electrode 18e can have a cut angle 68 that ranges from 1 to
20 60°, with preferred ranges of at least 25° or, at least 30° and specific embodiment of 25° and 30°. The surface of electrode 18e can be smooth or textured and concave or convex. Electrode 18e can have different lengths 38 that are advanced from distal end 16' of introducer 12. The lengths can be determined by the actual physical length of electrode(s) 18e, the length 38' of an
25 energy delivery surface 18eds of electrode 18e and the length, 38'' of electrode 18e that is covered by an insulator 36. Suitable lengths 38 include but are not limited to a range from 1-30 cms with specific embodiments of 0.5, 1, 3, 5, 10, 15 and 25.0 cm. The conductive surface area 18eds of electrode 18e can range from 0.05 mm² to 100 cm². The actual lengths of electrode 18e depend on the
30 location of tissue site 5' to be ablated, its distance from the site, its accessibility as well as whether or not the physician performs an endoscopic or surgical

procedure. While the conductive surface area 18eds depends on the desired ablation volume 5av to be created.

Referring now to Figures 17 and 18, electrode 18e can also be configured to be flexible and or deflectable having one or more radii of curvature 70 which can exceed 180° of curvature. In use, electrode 18e can be positioned to heat, necrose or ablate any selected target tissue volume 5'. A radiopaque marker 11 can be coated on electrodes 18e for visualization purposes. Electrode 18e can be coupled to introducer 12 and or an advancement member or device 15 or and advancement-retraction member 34 using soldering, brazing, welding, crimping, adhesive bonding and other joining methods known in the medical device arts. Also, electrode 18e can include one or more coupled sensors 22 to measure temperature and impedance (both of the electrode and surrounding tissue), voltage and current other physical properties of the electrode and adjacent tissue. Sensors 22 can be at exterior surfaces of electrodes 18e at their distal ends or intermediate sections.

Electrode 18e can be made of a variety of conductive materials, both metallic and non-metallic. Suitable materials for electrode 18e include, steel such as 304 stainless steel of hypodermic quality, platinum, gold, silver and alloys and combinations thereof. Also, electrode 18e can be made of conductive solid or hollow straight wires of various shapes such as round, flat, triangular, rectangular, hexagonal, elliptical and the like. In a specific embodiment all or portions of electrodes 18e or a second electrode 18e' can be made of a shaped memory metal, such as NiTi, commercially available from Raychem Corporation, Menlo Park, California.

Referring now to Figures 19 through 22, in various embodiments one or more resilient members 18 or electrodes 18e can be covered by an insulative layer 36 so as to have an exterior surface that is wholly or partially insulated and provide a non-insulated area which is an energy delivery surface 18eds. In an embodiment shown in Figure 19, insulative layer 36 can comprise a sleeve that can be fixed or slidably positioned along the length of electrode 18e to vary and control the length 36' of energy delivery surface 18eds. Suitable material for

insulative layer 36 includes polyamide and fluorocarbon polymers such as TEFLON.

5 In the embodiment shown in Figure 20, insulation 36 is formed at the exterior of electrodes 18e in circumferential patterns, leaving a plurality of energy delivery surfaces 18eds. In an embodiment shown in Figures 21 and 22, insulation 36 extends along a longitudinal exterior surface of electrodes 18e. Insulation 36 can extend along a selected distance along a longitudinal length of electrodes 18e and around a selectable portion of a circumference of electrodes 18e. In various embodiments, sections of electrodes 18e can have insulation 36 along selected longitudinal lengths of electrodes 18e as well as completely surround one or more circumferential sections of electrodes 18e. Insulation 36 positioned at the exterior of electrodes 18,18e can be varied to define any desired shape, size and geometry of energy delivery surface 18eds

10 Referring now to Figure 23, in various embodiments electrode 18e can include one or more lumens 72 (which can be contiguous with or the same as lumen 13) coupled to a plurality of fluid distribution ports 23 (which can be apertures 23) from which a variety of fluids 27 can be introduced, including conductivity enhancing fluids, electrolytic solutions, saline solutions, cooling fluids, cryogenic fluids, gases, chemotherapeutic agents, medicaments, gene therapy agents, photo-therapeutic agents, contrast agents, infusion media and combinations thereof. This is accomplished by having ports or apertures 23 that are fluidically coupled to one or more lumens 72 coupled to lumens 13 in turn coupled to fluid reservoir 30 and/or fluid delivery device 28.

15 In an embodiment shown in Figure 23, a conductivity enhancing solution 27 can be infused into target tissue site 5' including tissue mass 5''. The conductivity enhancing solution can be infused before during or after the delivery of energy to the tissue site by the energy delivery device. The infusion of a conductivity enhancing solution 27 into the target tissue 5' creates an infused tissue area 5i that has an increased electrical conductivity (verses un-infused tissue) so as to act as an enhanced electrode 40. During RF energy delivery, the current densities in enhanced electrode 40 are greatly lowered allowing the

delivery of greater amounts of RF power into electrode 40 and target tissue 5' without impedance failures. In use, the infusion of the target tissue site with conductivity enhancing solution provides two important benefits: (i) faster ablation times; and (ii) the creation of larger lesions; both without impedance-related shut downs of the RF power supply. This is due to the fact that the conductivity enhancing solution reduces current densities and prevents desiccation of tissue adjacent the electrode that would otherwise result in increases in tissue impedance. A preferred example of a conductivity enhancing solution is a hypertonic saline solution. Other examples include halide salt solutions, and colloidal-ferro solutions and colloidal-silver solutions. The conductivity of enhanced electrode 40 can be increased by control of the rate and amount of infusion and the use of solutions with greater concentrations of electrolytes (e.g. saline) and hence greater conductivity. In various embodiments, the use of conductivity enhancing solution 27 allows the delivery of up to 2000 watts of power into the tissue site impedance shut down, with specific embodiments of 50, 100, 150, 250, 500, 1000 and 1500 watts achieved by varying the flow, amount and concentration of infusion solution 27. The infusion of solution 27 can be continuous, pulsed or combinations thereof and can be controlled by a feedback control system described herein. In a specific embodiment, a bolus of infusion solution 27 is delivered prior to energy delivery followed by a continuous delivery initiated before or during energy delivery with energy delivery device 18e or other means.

Turning now to a discussion of impedance sensors, in various embodiments impedance sensor 22 can include all or a portion of resilient members 18. Referring back to Figure 19, when resilient member 18 is made of a conductive material the length 22l of impedance sensor 22 can be defined by the placement of a slidable or fixed insulative layer 36. Also in various embodiments impedance sensors 22 can be fabricated from a variety of conductive materials and metals known in the art including stainless steel, copper, silver, gold, platinum and alloys and combinations thereof. Referring now to Figure 24, similarly all or portions of sensors 22 or sensor members 22m can comprise

a conductive coating 22c that is coated or deposited onto a selected portion of member 18 using. In various embodiments, coating 22c can comprise a conductive metal or conductive polymer coating known in the art that is applied using known methods such as sputtering, vacuum deposition, dip coating, photolithography and the like. In a related embodiments, impedance sensing members 22m and/or sensor 22 can be configured to have a resistance gradient 22g along all or portions of their lengths 22l. The resistance gradient can be increasing or decreasing in a linear, second order, third order, exponential or other fashion. In a specific embodiment the resistance gradient is configured to compensate for resistance losses (i.e. of voltage) and/or hysteresis occurring along the length 22l of member 22m or sensor 22, as well as changes in the overall resistance of sensor 22 due to changes in the temperature and/or conducting/sensing length 22lc (and area) of sensor 22 as might occur due to advancement or retraction of slidable insulation layer, or fouling of the sensor with, desiccated, burnt tissue or otherwise adherent tissue. In this and related embodiments the gradient can be so configured to produce the least resistance (e.g. maximum conductance) at the distal tip 22d of the sensor 22 and increasing moving in a proximal direction along. The gradient can be produced via the use of coating 22c either by varying the thickness or composition of the coating, or a combination of both along the length 22l of the sensor using methods known in the art. Further, by compensating for such resistance changes or losses along the length or area of impedance sensor 22, these and related embodiments also improve the measurement and detection of real and imaginary components of complex impedance. In other related embodiments, the resistance gradient can be in a radial direction or a combination of radial and linear directions with respect to the sensor length 22l.

In other embodiments sensors 22 can comprise a number of biomedical sensors known in the art including but not limited to thermal sensors, acoustical sensors, optical sensors, pH sensors, gas sensors, flow sensors positional sensors and pressure/force sensors. Thermal sensors can include thermistors, thermocouples, resistive wires, optical sensors and the like. Acoustical sensors

can include ultrasound sensors including piezoelectric sensors which can be configured in an array. Pressure and force sensors can include strain gauge sensors including silicon-based strain gauges.

5 In an embodiment, sensor 22 can be selected to measure temperature along with impedance to compensate for any temperature related bias or hysteresis in the impedance measurement. Accordingly, in an embodiment a feedback signal from a temperature sensor or temperature calculation device 342 can be inputted to the impedance calculation device 334 described herein to compensate for such variation. Temperature monitoring can also be used to
10 perform real time monitoring of ablative energy delivery. If at any time sensor 22 determines that a desired cell necrosis temperature is exceeded, then an appropriate signal can be sent to power control circuitry describe herein to reduce or regulate the amount of electromagnetic energy delivered to electrodes 18 and 18'.

15 Referring now to Figures 25a-25c and 26a-26c, in an embodiment the position and size of an ablation volume 5av produced by the delivery of electromagnetic energy can be controlled via the frequency of the ablative energy delivered to one or more electrodes or energy delivery devices 18. As shown in Figure 26a, lower electromagnetic frequencies such as RF frequencies
20 (e.g. 1kHz to 1 MHZ) produce a more localized energy concentration (e.g. current density) with the resulting zone of energy concentration or ablation zone 5az occurring close to the energy delivery electrode/antenna in terms of a lateral distance 18dl or other direction. As shown in Figures 26b and 26c, higher frequencies such as microwave result in a progressively more distant energy
25 concentration and resulting ablation zone 5az. As shown in Figures 25a-25c, by varying the frequency of the delivered energy and/or utilizing energy delivery electrodes/antenna coupled to different frequency energy source (e.g. microwave vs. RF) the position, shape and size of the resulting lesion can be precisely controlled and even steered. This can be accomplished by electrically isolating
30 one or more electrodes 18 to allow for the use of separate frequencies for each electrode. Further, one or more isolated electrodes can be coupled to

5 multiplexing circuitry, and/or control resources coupled to the power sources and individual electrodes/antenna. Such circuitry and control resources can be used to turn individual electrodes or antenna off and on as well as control/set the frequency of each. In use, these and related embodiments provide the benefit of allowing the size, position and shape of the lesion to be precisely controlled and/or titrated to meet the therapeutic needs of the target tissue.

10 Referring now to Figures 25b and 25c, in various embodiments, one or more electrodes can have segmented portions 18sp so as to allow the electrodes to emit or radiate energy at different wavelengths from different segmented portions 18sp of electrode 18. Segmentation can be achieved through the use of electrically insulated sections 36s.

15 In an embodiment shown in Figure 25b, the use of segmented electrodes allows the creation of segmented ablation zones 5azs including a first and second segmented zone 5azs1 and 5azs2. The size and shape of the segmented ablation zones can be controlled by controlling the frequency of the delivered energy to each electrode segmented portion, 18sp. The segmented ablation zones can also be configured to be discontinuous or overlapping. Such embodiments also provide the ability to avoid injury to anatomical structure such as blood vessels, nerves etc., which lie in close proximity or are actually
20 surrounded by the tumor to be treated. For example, in an embodiment shown in Figure 25b, the segmented ablation zones 5azs1 and 5azs2 can be sized and positioned to have sufficient space between each zone to avoid damaging a blood vessel 5bv or other critical structure 5as which lies between two or more electrodes 18. Alternatively if desired, the ablative frequencies delivered to each
25 electrode segmented portion 18sp can be reconfigured to produce overlapping segmented ablation zones 5azs as is shown in Figure 25c

30 In use, the medical practitioner would position the apparatus and then image the target tissue site (using imaging systems known in the art such as ultrasound) to identify both the tumor and critical structures and then utilize that image to control the input frequency to the energy delivery device to produce the desired lesion size and shape to completely ablate the tumor while avoiding the

critical structure. In an embodiment, the image could be electronically stored and analyzed to identify tumors and surrounding anatomy (using imaging processing methods known in the art such as edge detection algorithms resident within a processor of the imaging device) with the output feed into a power control software module coupled to the power supply, that controls the power frequency to produce the desired ablation volume. Another benefit of these and related embodiments is the ability to produce an energy or thermal gradient within a target tissue site. That is the ability to deliver more or less energy to discrete sections of the target tissue volume in order to titrate the delivery of energy to address the physical and thermal conditions of a particular tumor mass and even subsections of the tumor mass. This is an important capability because tumors are often morphologically, and therefore thermally non-homogeneous, a problem which current ablative therapies have not recognized or addressed.

Exemplary embodiments for the use of this capability include delivering larger amounts of energy to the center of a tumor and less to periphery in order to produce higher temperatures and ensure complete ablation at the center and minimize risk of thermal injury to surrounding healthy tissue. Alternatively, increased energy could also be selectively directed to the tissue tract made by the RF needle or probe (or other penetrating energy delivery device) in penetrating the tumor and surrounding tissue to ensure that no living malignant tissue is dragged back through the tract upon removal of the RF needle.

Referring now to Figures 6 and 27, various embodiments of the invention can be configured to generate and display images or maps 4' from one or more impedance measurements including but not limited to complex impedance, impedance vectors, impedance loci and combinations thereof. In an embodiment, a process 100 for generating and displaying an impedance map or impedance derived image 4' includes one or more of the following steps, all or a portion of which, can be implemented as an electronic instruction set on a processor or logic resources described herein. Impedance array 22a and/or apparatus 10 can be positioned 101 within or near the desired sample volume 5sv and/or conductive paths 22cp can be selected 105 so as to define, and thus

select 110, a particular sample volume 5sv. The volume is then imaged 200 using all or a portion of the sensing members 22m or sensors 22 that comprise array 22a. A decision 300 can then be made to perform one or more re-images of the sample volume in order to enhance image resolution as needed. Further,
5 different excitation currents can be applied to the target tissue site and the voltage measurements repeated over time to increase measurement accuracy and precision through increased sampling and reducing signal bias or noise that may occur at a particular excitation current. Signals 22i from impedance array 22a can then be signaled or inputted 400 to logic resources 19lr include module 19m
10 which can include an image processing sub-module 19mi. Sub-module 19mi includes subroutines or algorithms configured to generate an impedance map or derived image 4' of all or a portion of the target tissue volume 5' using image/signal processing methods including, but not limited to, edge detection, filtering, approximating techniques, volume imaging, contrast enhancement,
15 fuzzy logic and other methods known in the art. Alternatively, one or more signals 22i from array 22a can be inputted or signaled 500 to memory resources 19mr (or an externally coupled data storage device) and stored as an impedance data set 22ds in memory resources 19mr. Subsequently, all or a portion of data set 22ds can be inputted to sub-module 19mi and processed 600 as described
20 herein to generate an impedance map or impedance derived image 4' which can then be displayed 700 on display device 21 or other display means. A decision 800 can then be made to image a new sample volume and the process can be repeated starting at steps 101 or 105. In an embodiment, the imaging or mapping process can be facilitated by rotating array 22a about introducer axis
25 12al or advancing and retracting one or more sensing members 22m from members 18 or a combination of both.

In an embodiment module 19m or 19mi can include an algorithm utilizing Laplace's equation to calculate impedivity or resistivity from the known voltages and currents measured at one or more conductive pathways 22cp within
30 the target tissue volume. Reference measurements or normalization methods may be used to account for noise in the measurements. In related embodiments

impedance and other bioelectric measurements described herein can be analyzed and converted from the frequency domain to the time using transform function including Fourier transforms, fast Fourier transforms, wavelet analysis methods and other numerical methods known in the art. These functions and methods
5 can be incorporated into algorithms or subroutine within module 19m or 19mi. These algorithms incorporating wavelet functions and transforms (including packets) can be configured to analyze and solve multidimensional and multi-frequency data and associated functions and equations. This approach provides the benefit of more flexibility in applying wavelets to analyze impedance,
10 conductivity and other bioelectric data gathered using systems and apparatus of the present invention. One or more of the following wavelet functions can be incorporated into an algorithm or subroutine of module 19m or 19mi: spline wavelets, waveform modeling and segmentation, time-frequency analysis, time-frequency localization, fast algorithms and filter banks, integral wavelet
15 transforms, multiresolution analysis, cardinal splines, orthonormal wavelets, orthogonal wavelet spaces, wavelets of haar, shannon, and meyer; spline wavelets of battle-lemarié and strömberg; the daubechies wavelets; biorthogonal wavelets, orthogonal decompositions and reconstruction; and multidimensional wavelet transforms. In an exemplary embodiment modules 19m or 19mi utilizes
20 spline wavelets to allow analysis and synthesis of discrete data on uniform or non-uniform tissue sample sites without any boundary effect.

Image module 19mi can also include subroutines to perform interpolation such as linear, quadratic or cubic spline interpolation between individual measured impedance values from image data set of a given sample volume.
25 This improves image quality including resolution without any substantial loss of spatial or contrast detail. In related embodiments the image processing module 19mi can be configured to allow the user to select both the interpolative or other image processing algorithms to be performed as well as the area of the image to be so processed. Thus the user can select all or a portion of the image to
30 enhanced providing faster image processing times (by not having to process the entire image) as well improving image quality and other overall usability of the

imaging apparatus/system. The image processing module 19mi can also include gray scale and color contrast capabilities which can be selectable. Both the gray scale and color can be scaled or normalized against a baseline measurement obtained from the individual patient, a calibration measurement or a statistic (e.g. mean) value for a patient sample group or a parameter (e.g. average) for a patient population or a combination thereof.

In related embodiments monitoring apparatus 19 and module 19mi can be configured to generate impedance images with the maximum visual distinction or contrast between tumorous tissue and healthy tissue. This can be accomplished by using the frequency or combination of frequencies that yield the maximum sensitivity for selected tissue types or tissue conditions indicative of a tumor (e.g. degree of vascularity temperature etc). In an embodiment such frequencies can be determined by performing swept frequency measurements and generating an impedance map or image using one or more frequencies which resulted in the best contrast between healthy tissue and tumorous tissue or other tissue condition (e.g. thermal injury, necrosis etc.).

Referring now to Figures 28 and 29, a feedback control system 329 can be connected to energy source 320, sensors 324 impedance array 322a and energy delivery devices 314 and 316. Feedback control system 329 receives temperature or impedance data from sensors 324 and the amount of electromagnetic energy received by energy delivery devices 314 and 316 is modified from an initial setting of ablation energy output, ablation time, temperature, and current density (the "Four Parameters"). Feedback control system 329 can automatically change any of the Four Parameters. Feedback control system 329 can detect impedance or temperature and change any of the Four Parameters in response to either or a combination. Feedback control system 329 can include a multiplexer (digital or analog) to multiplex different electrodes, sensors, sensor arrays and a temperature detection circuit that provides a control signal representative of temperature or impedance detected at one or more sensors 324. A microprocessor can be connected to the temperature control circuit.

The following discussion pertains particularly to the use of an RF energy as an ablative energy source for apparatus 10. For purposes of this discussion, energy delivery devices 314 and 316 will now be referred to as RF electrodes/antennas 314 and 316 and energy source 320 will now be an RF energy source. However it will be appreciated that all other energy delivery devices and sources discussed herein are equally applicable and devices similar to those associated with biopsy treatment apparatus 10 can be utilized with laser optical fibers, microwave devices and the like. The temperature of the tissue, or of RF electrodes 314 and 316 is monitored, and the output power of energy source 320 adjusted accordingly. The physician can, if desired, override the closed or open loop system.

The user of apparatus 10 can input an impedance value that corresponds to a setting position located at apparatus 10. Based on this value, along with measured impedance values, feedback control system 329 determines an optimal power and time needed in the delivery of RF energy. Temperature is also sensed for monitoring and feedback purposes. Temperature can be maintained to a certain level by having feedback control system 329 adjust the power output automatically to maintain that level.

In another embodiment, feedback control system 329 determines an optimal power and time for a baseline setting. Ablation volumes or lesions are formed at the baseline first. Larger lesions can be obtained by extending the time of ablation after a center core is formed at the baseline. The completion of lesion creation can be checked by advancing energy delivery device 316 from distal end 16' of introducer 12 to a position corresponding to a desired lesion size and monitoring the temperature at the periphery of the lesion such that a temperature sufficient to produce a lesion is attained.

The closed loop system 329 can also utilize a controller 338 to monitor the temperature, adjust the RF power, analyze the result, refeed the result, and then modulate the power. More specifically, controller 338 governs the power levels, cycles, and duration that the RF energy is distributed to electrodes 314 and 316 to achieve and maintain power levels appropriate to achieve the desired

treatment objectives and clinical endpoints. Controller 338 can also in tandem analyze spectral profile 19p and perform tissue biopsy identification and ablation monitoring functions including endpoint determination. Further, controller 338 can in tandem govern the delivery of electrolytic, cooling fluid and, the removal of aspirated tissue. Controller 338 can be integral to or otherwise coupled to power source 320. In this and related embodiments, controller 338 can be coupled to a separate impedance measurement current source 317 and can be configured to synchronize the delivery of pulsed power to tissue site to allow for sensing by sensors or sensor array 322a during off power off intervals to prevent or minimize signal interference, artifacts or unwanted tissue effects during sampling by sensors 324 or sensor array 322a. The controller 338 can also be coupled to an input/output (I/O) device such as a keyboard, touchpad, PDA, microphone (coupled to speech recognition software resident in controller 338 or other computer) and the like. In an embodiment current source 317 can be a multi-frequency generator such as those manufactured by the Hewlett Packard Corporation (Palo Alto, California) and can include or be coupled to a spectrum analyzer manufactured by the same company.

Referring now to Figure 28, all or portions of feedback control system 329 are illustrated. Current delivered through RF electrodes 314 and 316 (also called primary and secondary RF electrodes/antennas 314 and 316) is measured by a current sensor 330. Voltage is measured by voltage sensor 332. Impedance and power are then calculated at power and impedance calculation device 334. These values can then be displayed at a user interface and display 336. Signals representative of power and impedance values are received by controller 338 which can be a microprocessor 338.

A control signal is generated by controller 338 that is proportional to the difference between an actual measured value and a desired value. The control signal is used by power circuits 340 to adjust the power output in an appropriate amount in order to maintain the desired power delivered at the respective primary and/or secondary antennas 314 and 316. In a similar manner,

temperatures detected at sensors 324 provide feedback for maintaining a selected power. The actual temperatures are measured at temperature measurement device 342, and the temperatures are displayed at user interface and display 336. A control signal is generated by controller 338 that is

5 proportional to the difference between an actual measured temperature, and a desired temperature. The control signal is used by power circuits 340 to adjust the power output in an appropriate amount in order to maintain the desired temperature delivered at the respective sensor 324. A multiplexer 346 can be included to measure current, voltage and temperature, at the numerous sensors

10 324 as well as deliver and distribute energy between primary electrodes 314 and secondary electrodes 316. Suitable multiplexers include but are not limited to those manufactured by the National Semiconductor® Corporation (Santa Clara, Ca.) such as the CLC 522 and CLC 533 series; and those manufactured the Analog Devices® Corporation (Norwood, Mass).

15 Controller 338 can be a digital or analog controller, or a computer with embedded, resident or otherwise coupled software. In an embodiment controller 338 can be a Pentium® family microprocessor manufacture by the Intel® Corporation (Santa Clara, Ca). When controller 338 is a computer it can include a CPU coupled through a system bus. On this system can be a keyboard, a disk

20 drive, or other non-volatile memory systems, a display, and other peripherals, as are known in the art. Also coupled to the bus are a program memory and a data memory. In various embodiments, controller 338 can be coupled to imaging systems, including but not limited to ultrasound, CT scanners (including fast CT scanners such as those manufacture by the Imatron® Corporation (South San

25 Francisco, CA), X-ray, MRI, mammographic X-ray and the like. Further, direct visualization and tactile imaging can be utilized.

User interface and display 336 can include operator controls and a display. In an embodiment user interface 336 can be a PDA device known in the art such as a Palm® family computer manufactured by Palm® Computing

30 (Santa Clara, Ca). Interface 336 can be configured to allow the user to input control and processing variables, to enable the controller to generate appropriate

command signals. Interface 336 can also receives real time processing feedback information from one or more sensors 324 for processing by controller 338, to govern the delivery and distribution of energy, fluid etc.

5 The output of current sensor 330 and voltage sensor 332 is used by controller 338 to maintain a selected power level at primary and secondary antennas 314 and 316. The amount of RF energy delivered controls the amount of power. A profile of power delivered can be incorporated in controller 338, and a preset amount of energy to be delivered can also be profiled.

10 Circuitry, software and feedback to controller 338 results in process control, and the maintenance of the selected power, and are used to change, (i) the selected power, including RF, microwave, laser and the like, (ii) the duty cycle (on-off and wattage), (iii) bipolar or monopolar energy delivery and (iv) infusion medium delivery, including flow rate and pressure. These process variables are controlled and varied, while maintaining the desired delivery of power independent of changes in voltage or current, based on temperatures
15 monitored at sensors 324. A controller 338 can be incorporated into feedback control system 329 to switch power on and off, as well as modulate the power. Also, with the use of sensor 324 and feedback control system 329, tissue adjacent to RF electrodes 314 and 316 can be maintained at a desired
20 temperature for a selected period of time without causing a shut down of the power circuit to electrode 314 due to the development of excessive electrical impedance at electrode 314 or adjacent tissue.

 Referring now to Figure 29, current sensor 330 and voltage sensor 332 are connected to the input of an analog amplifier 344. Analog amplifier 344 can
25 be a conventional differential amplifier circuit for use with sensors 324. The output of analog amplifier 344 is sequentially connected by an analog multiplexer 346 to the input of A/D converter 348. The output of analog amplifier 344 is a voltage which represents the respective sensed temperatures. Digitized amplifier output voltages are supplied by A/D converter 348 to a
30 microprocessor 350. Microprocessor 350 may be a Power PC® chip available from Motorola or an Intel® Pentium® Series chip. However, it will be

appreciated that any suitable microprocessor or general purpose digital or analog computer can be used to calculate impedance or temperature or perform image processing and tissue identification functions.

Microprocessor 350 sequentially receives and stores digital
5 representations of impedance and temperature. Each digital value received by microprocessor 350 corresponds to different temperatures and impedances. Calculated power and impedance values can be indicated on user interface and display 336. Alternatively, or in addition to the numerical indication of power or impedance, calculated impedance and power values can be compared by
10 microprocessor 350 with power and impedance limits. When the values exceed predetermined power or impedance values, a warning can be given on user interface and display 336, and additionally, the delivery of RF energy can be reduced, modified or interrupted. A control signal from microprocessor 350 can modify the power level supplied by energy source 320 to RF electrodes 314 and
15 316. In a similar manner, temperatures detected at sensors 324 provide feedback for determining the extent and rate of (i) tissue hyperthermia (ii) cell necrosis; and (iii) when a boundary of desired cell necrosis has reached the physical location of sensors 324.

Referring now to Figure 30, in an embodiment one or more of
20 impedance measurement device 19, power supply 20, display device 21 and control system 329, controller 338 can be incorporated or integrated into a single control and display device or unit 20cd. Device 20cd can be configured to include display one or more of the following: impedance profile 19p, tissue site image 4', tumor volume image 4'', ablation volume image 4av, time temperature
25 profiles, tissue identification information, and ablation setting information (e.g. power setting, delivery time etc.). Device 20cd can also be configured to superimpose ablation volume image 4av onto tumor volume image 4'' or tissue site image 4' as well as superimpose visual cues 4c on the placement (including proper and improper placement) of apparatus 10 including energy delivery
30 devices 18e within the tumor volume 5'' or tissue site 5''. Device 20cd can also

include controls knobs 20ck for manipulating any of the images (4', 4" or 4av) in one or more axis.

Referring now to Figure 31, in various embodiments impedance measurement device 19 or control system 329 can be configured to switch from a first mode of measuring impedance to a second mode when certain system impedance or power conditions occur. In an embodiment, the first mode of measuring impedance is done utilizing the RF treatment power and then impedance is calculated using a measured current and voltage as described herein. However, when system impedance rises too greatly and the resulting RF power treatment power level drops below a threshold, the accuracy and precision of localized impedance measurements decreases as a result of the decrease in the impedance measurement current in relation to noise levels of the RF power system. This is a problem not recognized nor addressed by current RF ablative and related impedance measurement devices. Under such conditions logic resources 19lr within monitoring device 19 can be configured to switch to a second mode of measuring localized impedance. The threshold event causing the mode switching can be selectable and include one or more of the following events: decreases in treatment (e.g. RF) power below a threshold level 20pt, increases in system impedance above a threshold level 20it, changes in slope (e.g. derivative) of the RF power or system impedance curves. In various embodiments, the threshold level 20pt of RF treatment power 20t causing mode switching can be in the range from 1 to 50 watts with specific embodiments of 5, 10 and 25 watts.

In an embodiment shown in Figure 31, this second or alternative mode of measuring impedance can comprise superimposing a duty cycled measurement signal 20e onto the treatment signal 20t. The pulse duration 20pd of signal 20e can be in the range of 1 to 500 ms with specific embodiments of 50, 100 and 250 ms. The duty cycle 20dc of signal 20e can be in the range from 1 to 99% with specific embodiments of 10, 25, 50 and 75%. Monitoring device 19, power source 20 or control system 329 can be configured to control the power amplitude of the measurement signal to maintain a selected total signal

amplitude 20at. In an embodiment the total signal amplitude 20at can range from about 5 to about 50 watts, with specific embodiments of 10, 20, 30 and 40 watts. Also the duty cycle, pulse duration and total signal amplitude can be controlled to deliver a selectable average power over the duty cycle which can be in the range of about 0.5 to about 10 watts with specific embodiments 1, 2, 5 and 5 watts. By controlling the average power delivered over the duty cycle, higher measurement currents can be used in short pulse duration without appreciably affecting delivered treatment power, system performance or causing additional or unwanted energy delivery to the target tissue site.

In use, these and related embodiments of alternative measurement of impedance measurements including superimposed duty cycle measurement, provide the benefit of improved accuracy and signal to noise ratios of impedance and related bio-electric measurements under conditions of high system impedance and/or lower levels of delivered RF treatment power (i.e. ablative power).

In related embodiments, the duty cycle and/or pulse duration can be configured to vary responsive to one or more selected parameters which can include frequency of the treatment signal, power of the treatment signal, or impedance of the treatment signal. The variation in either the pulse duration or duty cycle can be controlled by control system 329 and/or logic resources of the impedance monitoring device or power supply using control methods known in the art such as PID control. In use, these embodiments allow the impedance measurements to be continuously fine tuned to changing system conditions to improve the accuracy and precision of impedance and related bioelectric measurements.

Conclusion:

It will be appreciated that the applicants have provided a novel and useful apparatus and method for the diagnosis and treatment of tumors using minimally invasive methods including tissue impedance measurements. The foregoing description of various embodiment of the invention has been

presented for purposes of illustration and description. It is not intended to be exhaustive or to limit the invention to the precise forms disclosed.

Embodiments of the invention can be configured for the treatment of tumor and tissue masses at or beneath a tissue surface in a number of organs including but
5 no limited to the liver, breast, bone and lung. However, embodiments of the invention are applicable to other organs and tissue as well. Obviously, many modifications and variations will be apparent to practitioners skilled in this art. Further, elements from one embodiment can be readily recombined with elements from one or more other embodiments. Such combinations can form a
10 number of embodiments within the scope of the invention. It is intended that the scope of the invention be defined by the following appended claims and their equivalents. Moreover, various other aspects of the invention disclosed herein are set out in the following numbered clauses:

- 15 1. A method for detecting and treating a tumor using tissue localized volumetric impedance measurements, the method comprising:
 - providing an impedance measurement apparatus including an impedance sensor array having a plurality of resilient members deployable with curvature and configured to sample tissue impedance through a plurality of conductive
20 pathways, the apparatus configured to be coupled to at least one of an energy delivery device, a power supply, a switching device or logic resources;
 - positioning the apparatus at a selected tissue site;
 - deploying the impedance array to define a sample volume;
 - utilizing the impedance array to make impedance measurements through
25 a plurality of conductive pathways;
 - determining a tissue condition of the sample volume utilizing information from the impedance measurements; and
 - delivering energy from the energy delivery device to ablate or necrose at
30 least a portion of the tumor.

2. A method of detecting and treating a tumor utilizing volumetric complex impedance measurement, the method comprising:

providing a tissue diagnosis and treatment apparatus for detecting and treating a tumor, the apparatus including, an impedance sensor array, the apparatus configured to be coupled to at least one of an energy delivery device,
5 a power supply, logic resources or a switching device;

introducing the apparatus into a target tissue site;

positioning the sensor array to define a sample volume;

making a complex impedance measurement within the sample volume;

10 and

analyzing real and imaginary components of the complex impedance measurement to determine a tissue condition of the sample volume.

What is claimed is:

15

CLAIMS

1. An apparatus for multi-pathway impedance characterization and
5 ablative treatment of tumors, the apparatus comprising:

an elongated delivery device including a lumen, the elongated delivery
device being maneuverable in tissue;

an impedance sensor array deployable from the elongated delivery
device and configured to be coupled to at least one of an electromagnetic energy
10 source or a switching device, the impedance array including a plurality of
resilient members, at least one of the plurality of resilient members being
positionable in the elongated delivery device in a compacted state and
deployable with curvature into tissue from the elongated delivery device in a
deployed state, the plurality of resilient members defining a sample volume in
15 the deployed state, at least one of the plurality of resilient members including
an impedance sensor, at least a portion of the impedance array configured to
sample tissue impedance through a plurality of conductive pathways;

an energy delivery device coupled to one of the sensor array, the at least
one resilient member or the elongated delivery device, the energy delivery
20 device including at least one RF electrode; and

an advancement member coupled to the impedance array, the
advancement member including an actuable portion, the advancement member
configured to control deployment of at least a portion of the array.

25 2. An apparatus for vector impedance characterization and ablative
treatment of tumors:

an elongated delivery device including a lumen, the elongated delivery
device being maneuverable in tissue;

an impedance sensor array deployable from the elongated delivery
30 device and configured to be coupled to at least one of an electromagnetic energy
source or a switching device, the impedance array including a plurality of

resilient members, at least one of the plurality of resilient members being positionable in the elongated delivery device in a compacted state and deployable with curvature into tissue from the elongated delivery device in a deployed state, the plurality of resilient members defining a sample volume in the deployed state, at least one of the plurality of resilient members including an impedance sensor, at least a portion of the impedance array configured to measure an impedance vector within a selectable tissue site;

an energy delivery device coupled to one of the sensor array, the at least one resilient member or the elongated delivery device, the energy delivery device including at least one electrode or antenna; and

an advancement member coupled to the energy delivery device, the advancement member including an actuatable portion, the advancement member configured to control deployment of at least a portion of the energy delivery device.

3. The apparatus of claim 1 or 2, wherein the plurality of resilient members includes a first, a second and a third resilient member.

4. The apparatus of claim 1 or 2, wherein the sensor has a resistance gradient or a resistance gradient configured to improve measurement of a complex impedance.

5. The apparatus of claim 4, wherein the resistance gradient is along a length of the sensor and configured compensate for resistive losses or hysteresis along the length of the sensor.

6. The apparatus of claim 1 or 2, at least a portion of the impedance arrays is configured to measure at least one of an intracellular impedance, an interstitial impedance or an intercellular capacitance.

7. The apparatus of claim 1 or 2, wherein the impedance array is configured to determine a locus of impedance within the sample volume.

8. The apparatus of claim 1 or 2, wherein the impedance array is configured to sample an impedance of at least a portion of the sample volume.

9. The apparatus of claim 8, wherein the at least a portion includes a first portion and a second portion.

10. The apparatus of claim 9, wherein the impedance array is configured to substantially simultaneously measure a first impedance profile of the first portion and second impedance profile of the second portion.

11. The apparatus of claim 1, wherein the plurality of conductive pathways are configured to be substantially evenly distributed or spaced within the sample volume.

12. The apparatus of claim 1, wherein the plurality of conductive pathways includes a first pathway and a second pathway.

13. The apparatus of claim 12, wherein the impedance array is configured to substantially simultaneously measure a first impedance of the first pathway and second impedance of the second pathway.

14. The apparatus of claim 12, the first pathway is positioned at a selectable angle relative to the second pathway.

15. The apparatus of claim 12, wherein the first and second pathway have no common segments.

16. The apparatus of claim 12, wherein the first and second pathway have a common origin.

5 17. The apparatus of claim 12, wherein the first and second pathway have substantially the same pathway, the second pathway being in an opposite direction to the first pathway.

10 18. The apparatus of claim 1 or 2, wherein the impedance array is configured to detect at an indicator of cell necrosis.

19. The apparatus of claim 1 or 2, wherein the impedance array is configured to detect at least one of a tissue ablation volume, a cell necrosis volume, a tissue thermal volume or a tissue hyperthermic volume.

15 20. The apparatus of claim 1 or 2, further comprising:
logic resources coupled to one of at least a portion of the impedance array, the energy delivery device, the switching device or the electromagnetic source, the logic resources including a processor.

20 21. The apparatus of claim 20, wherein one of the impedance array or logic resources is configured to measure or analyze tissue impedance or complex impedance at a measurement frequency distinct from an RF ablation frequency.

25 22. The apparatus of claim 20, wherein the logic resources are configured to identify a tissue condition or differentiate tissue responsive to an impedance signal from the at least a portion of the impedance array.

30 23. The apparatus of claim 22, wherein the logic resources are configured to analyze the signal at a frequency having an increased tissue condition sensitivity relative to a frequency spectrum.

24. The apparatus of claim 20, wherein the logic resources are configured to distinguish between normal and abnormal tissue, the abnormal tissue including at least one of abnormally mutated tissue, abnormally dividing
5 tissue, cancerous tissue, metastatic tissue or hypoxic tissue.

25. The apparatus of claim 20, wherein the logic resources are configured to distinguish between necrosed and non-necrosed tissue.

10 26. The apparatus of claim 20, wherein the logic resources are configured to analyze at least one of an intracellular impedance, an interstitial impedance an intercellular capacitance or a complex impedance.

15 27. The apparatus of claim 20, wherein the logic resources are configured to identify one of an inflection point, an asymptote, a minimum or a maximum of an impedance signal.

20 28. The apparatus of claim 27, wherein the logic resources are configured to identify at least one of an endpoint, an amount of tissue injury or a tissue type utilizing at least one of the inflection point, the asymptote, the minimum or the maximum of the impedance signal.

25 29. The apparatus of claim 20, wherein the logic resources are configured to identify an endpoint for an ablation procedure responsive to an impedance signal from the at least a portion of the impedance array.

30 30. The apparatus of claim 22, wherein the impedance signal includes at least one of an intracellular impedance, an interstitial impedance an intercellular capacitance or a complex impedance, the logic resources configured to identify a tissue condition utilizing at least one of an impedance

ratio including at least one of interstitial to intercellular impedance, real to imaginary impedance or impedance to capacitance.

5 31. The apparatus of claim 22, wherein the impedance signal is a complex impedance and the logic resources are configured to identify a tissue condition of the sample volume utilizing real and imaginary components of the complex impedance signal.

10 32. The apparatus of claim 20, wherein the impedance array is configured to substantially simultaneously measure an impedance of a first tissue volume portion and a second tissue volume portion and the logic resources are configured to compare the impedance of the first portion to an impedance of the second portion.

15 33. The apparatus of claim 2, the impedance array is configured to detect real and imaginary components of the impedance vector or magnitude and phase angle of the impedance vector.

20 34. An apparatus for multi-pathway impedance characterization and ablative treatment of tumors, the apparatus comprising:
 an elongated delivery device including a lumen, the elongated delivery device being maneuverable in tissue;
 an impedance sensor array deployable from the elongated delivery device and configured to be coupled to at least one of an electromagnetic energy
25 source or a switching device, the impedance array including a plurality of resilient members, at least one of the plurality of resilient members being positionable in the elongated delivery device in a compacted state and deployable with curvature into tissue from the elongated delivery device in a deployed state, the plurality of resilient members defining a sample volume in
30 the deployed state, at least one of the plurality of resilient members including

an impedance sensor, at least a portion of the impedance array configured to sample tissue impedance through a plurality of conductive pathways; and
an energy delivery device coupled to one of the sensor array, the at least one resilient member or the elongated delivery device, the energy delivery device including at least one electrode or antenna.

35. An apparatus for complex impedance characterization of tumors, the apparatus comprising:

an introducer including a lumen, the introducer being maneuverable in tissue; and

an impedance sensor array positionable in the introducer in a compacted state and deployable from the introducer to define a sample volume in a deployed state, the impedance array configured to be coupled to at least one of an electromagnetic energy source, logic resources or a switching device, the impedance array defining a sample volume in a deployed state, at least a portion of the impedance array configured to sample a complex tissue impedance through a plurality of conductive pathways and detect or measure an indicator of at least one of tumorous tissue or cell necrosis.

36. The apparatus of claim 35, wherein the impedance array includes a sensor, the sensor having one of a resistance gradient or a resistance gradient configured to improve measurement of a complex impedance.

37. An apparatus for impedance characterization and frequency directed RF ablative treatment of tumors, the apparatus comprising:

an elongated delivery device including a lumen, the elongated delivery device being maneuverable in tissue;

an impedance sensor array deployable from the elongated delivery device and configured to be coupled to at least one of an electromagnetic energy source or a switching device, the impedance array including a plurality of resilient members, at least one of the plurality of resilient members being

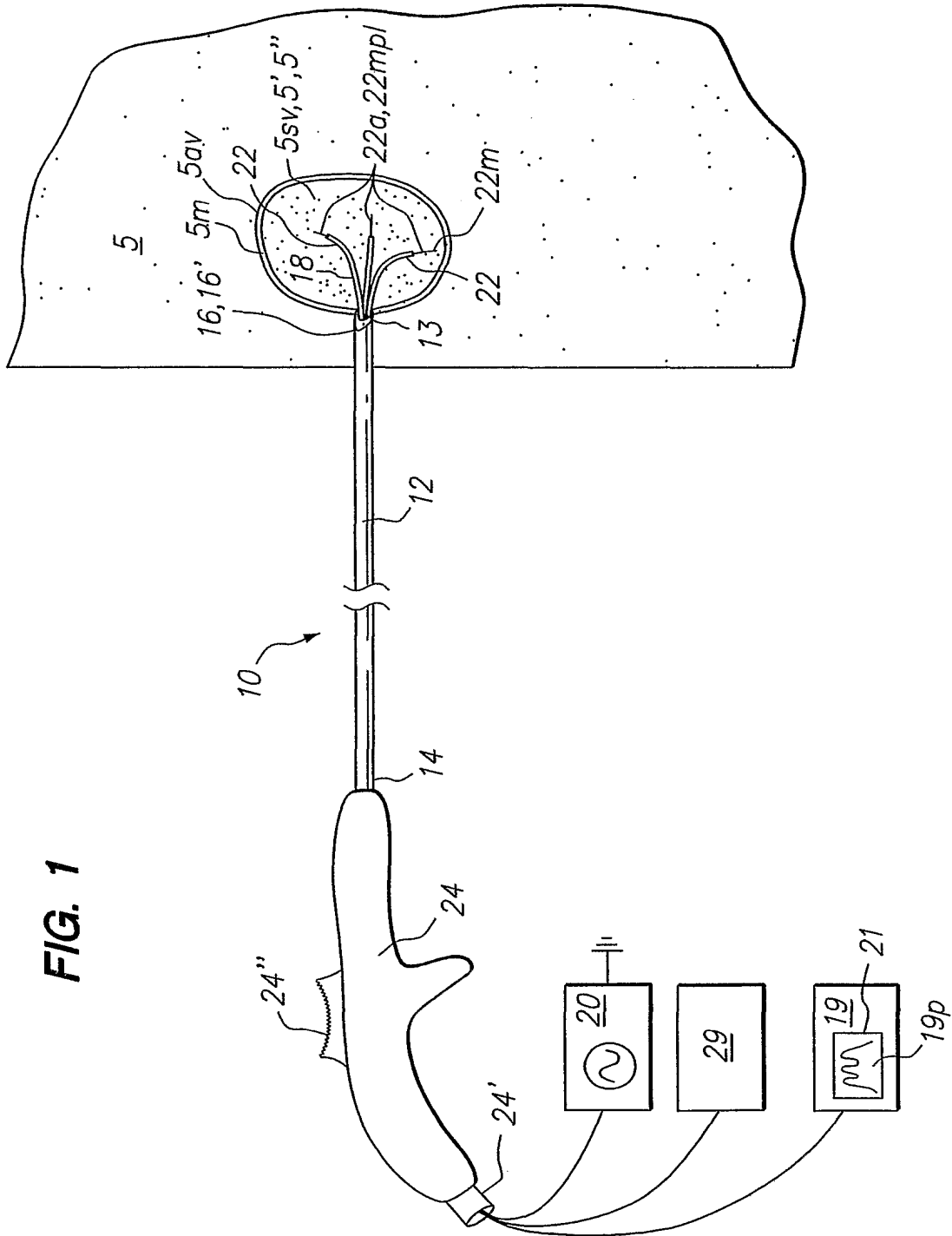
positionable in the elongated delivery device in a compacted state and
deployable with curvature into tissue from the elongated delivery device in a
deployed state, the plurality of resilient members defining a sample volume in
the deployed state, at least one of the plurality of resilient members including
5 an impedance sensor; and

an energy delivery device coupled to one of the sensor array, the at least
one resilient member or the elongated delivery device, the energy delivery
device including a plurality of RF electrodes configured to generate a
directional ablation zone responsive to an RF frequency.

10

1/26

FIG. 1



2/26

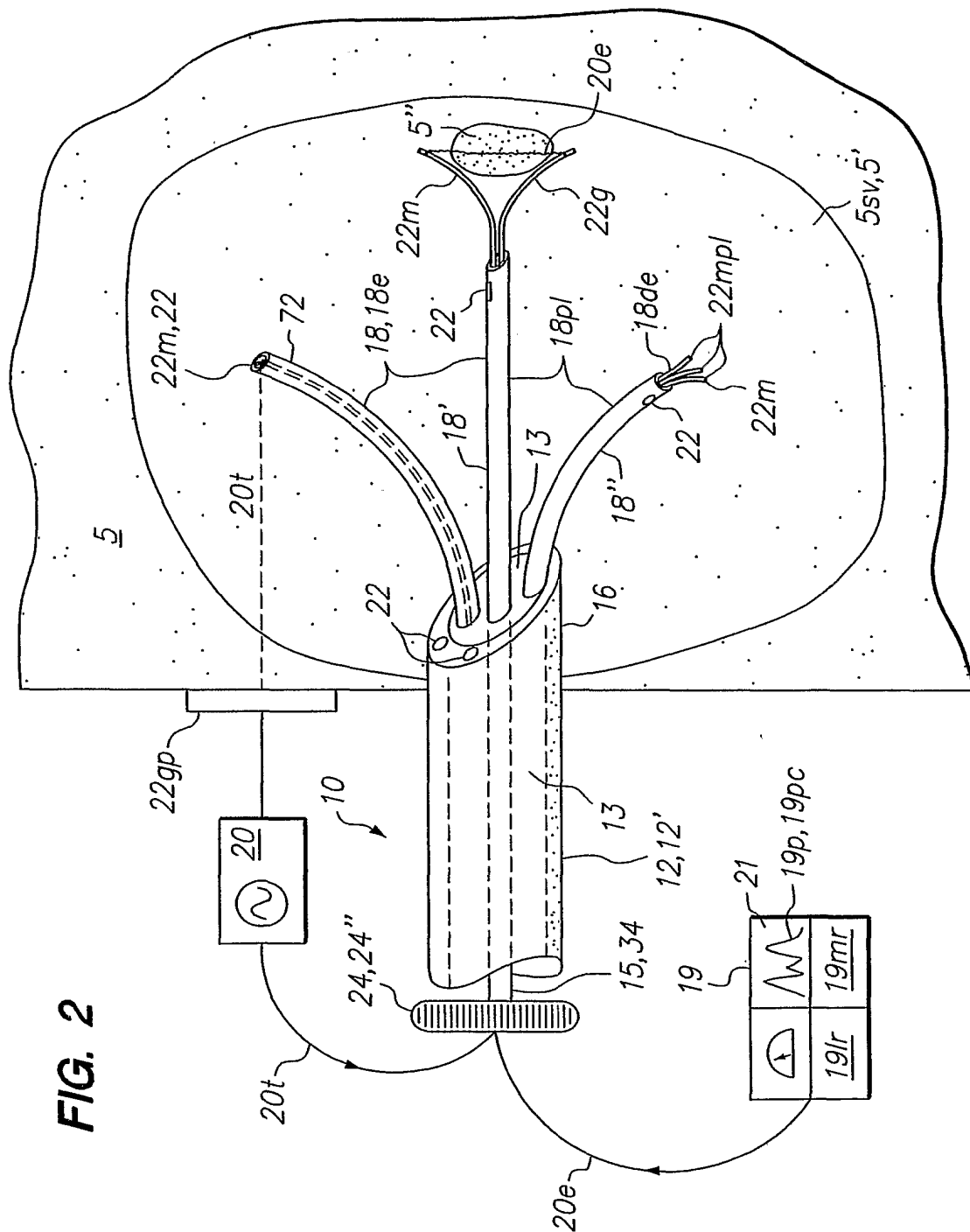


FIG. 2

3/26

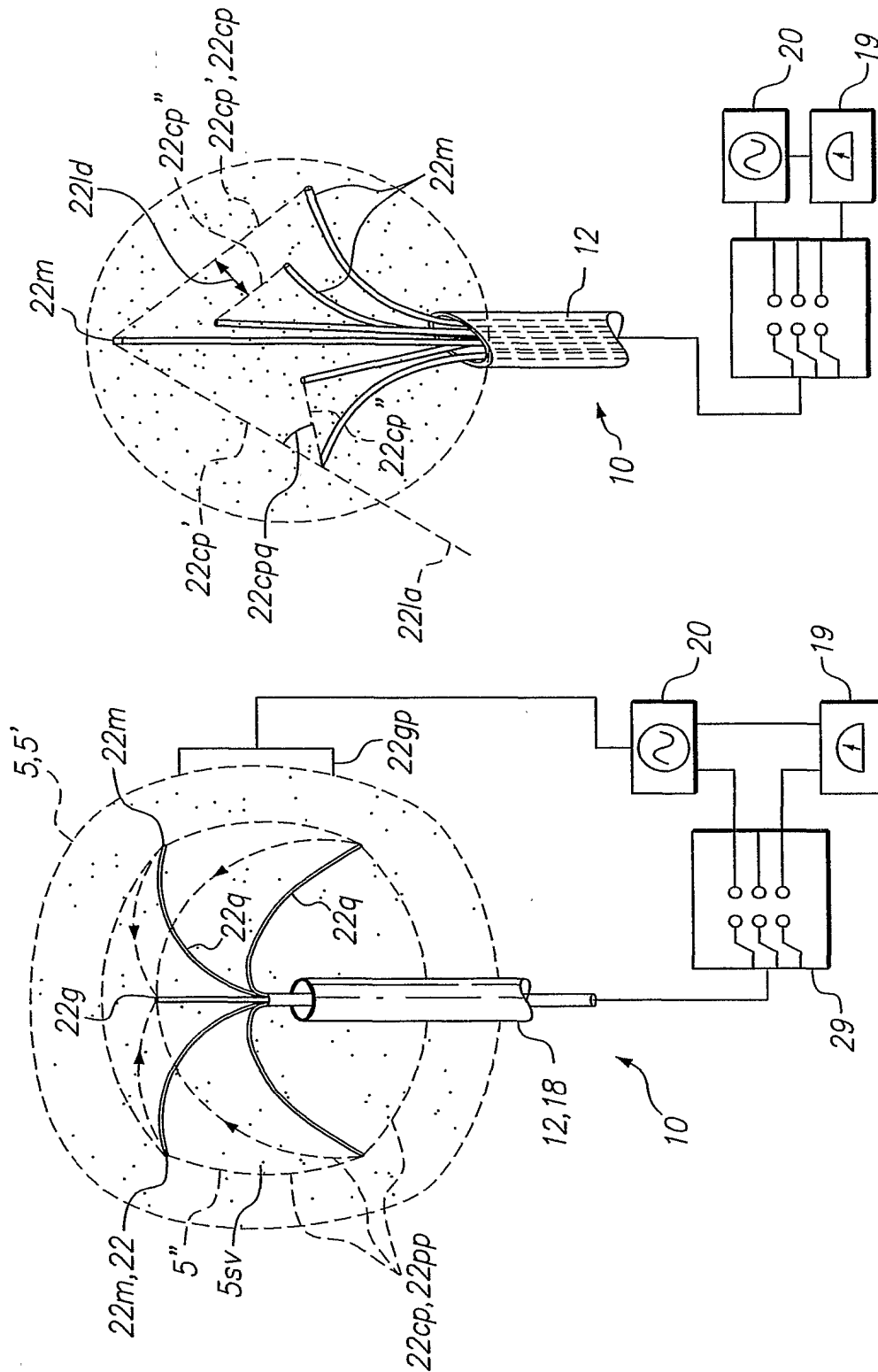


FIG. 3B

FIG. 3A

4/26

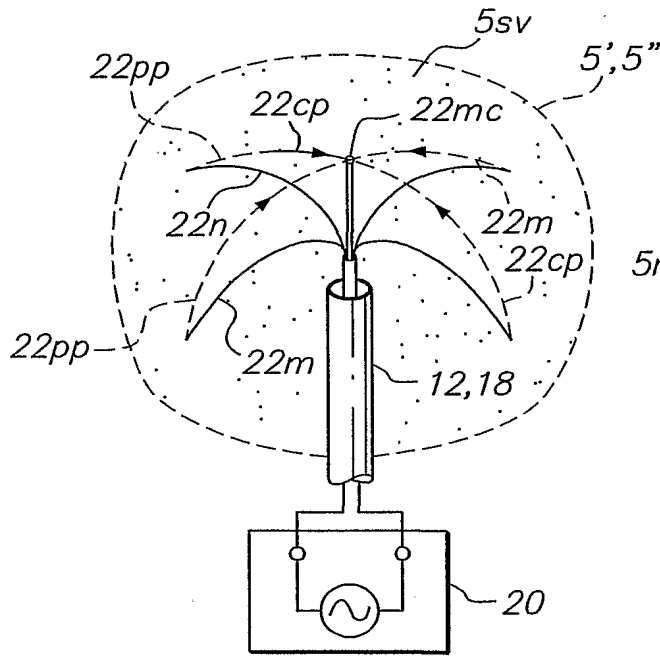


FIG. 4A

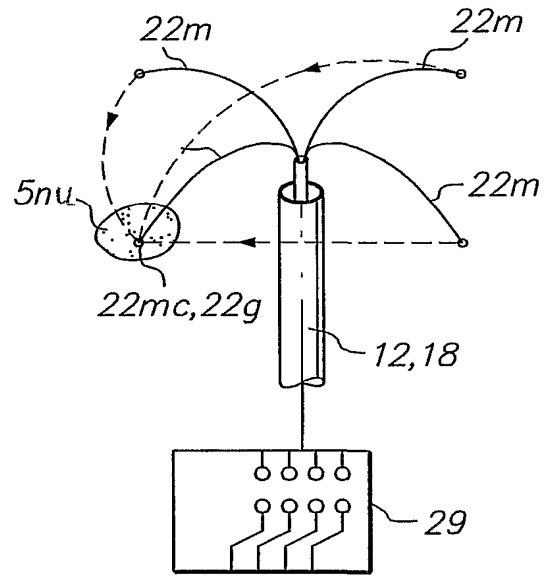


FIG. 4B

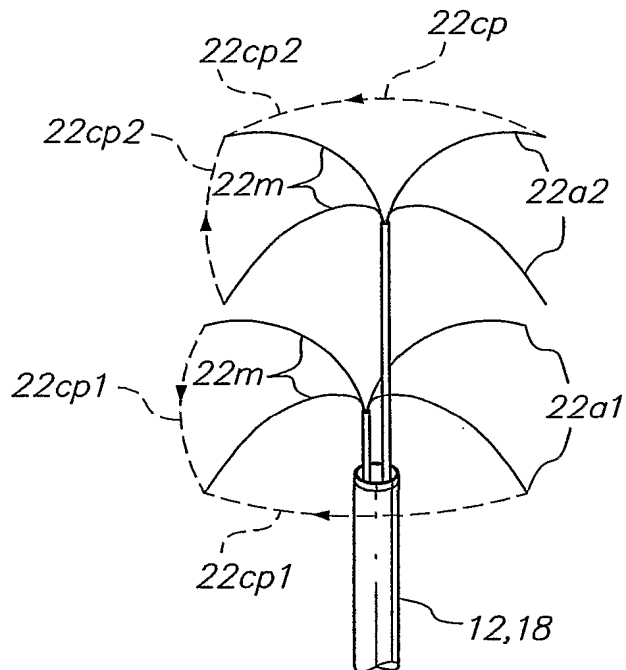


FIG. 4C

5/26

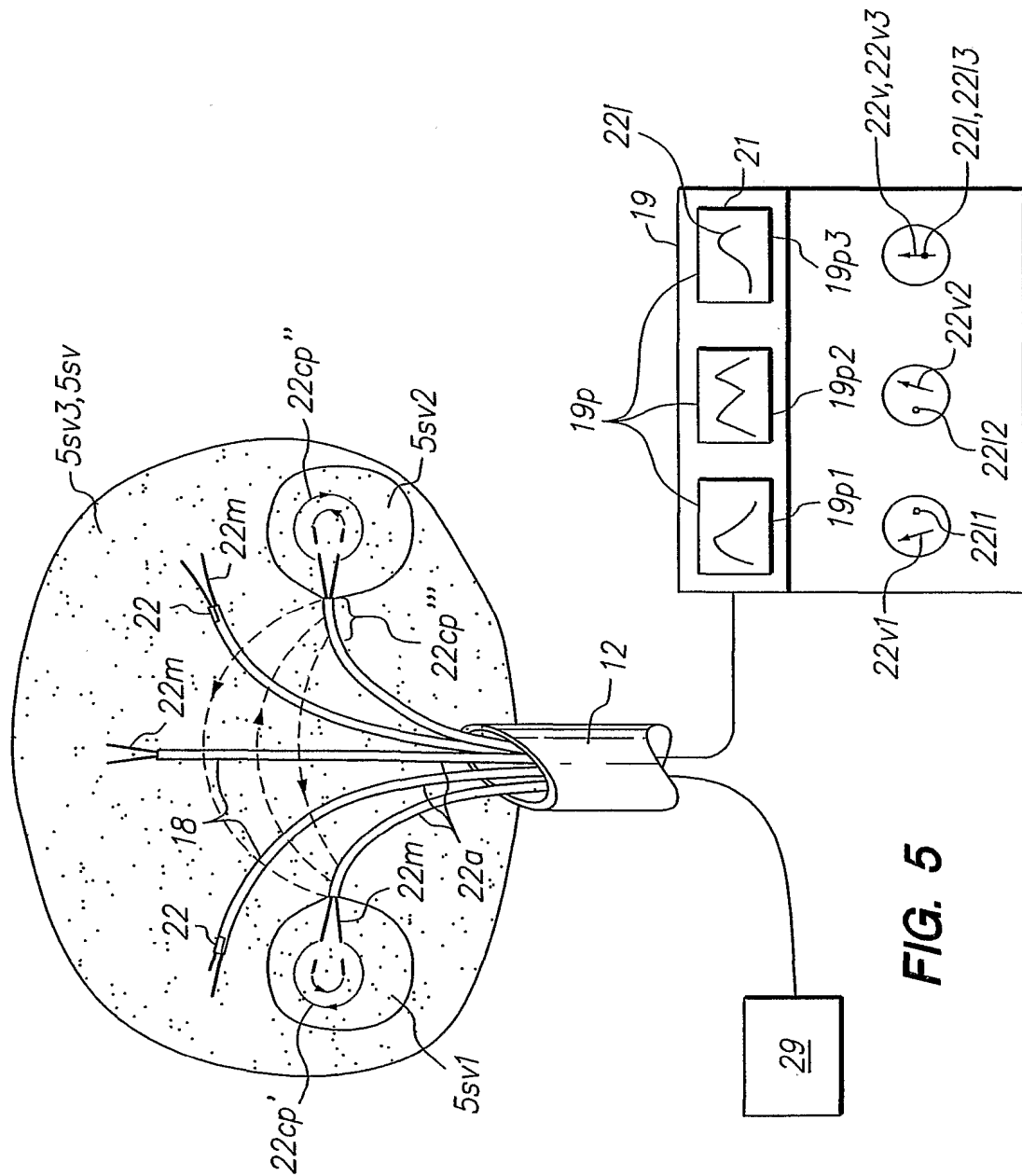
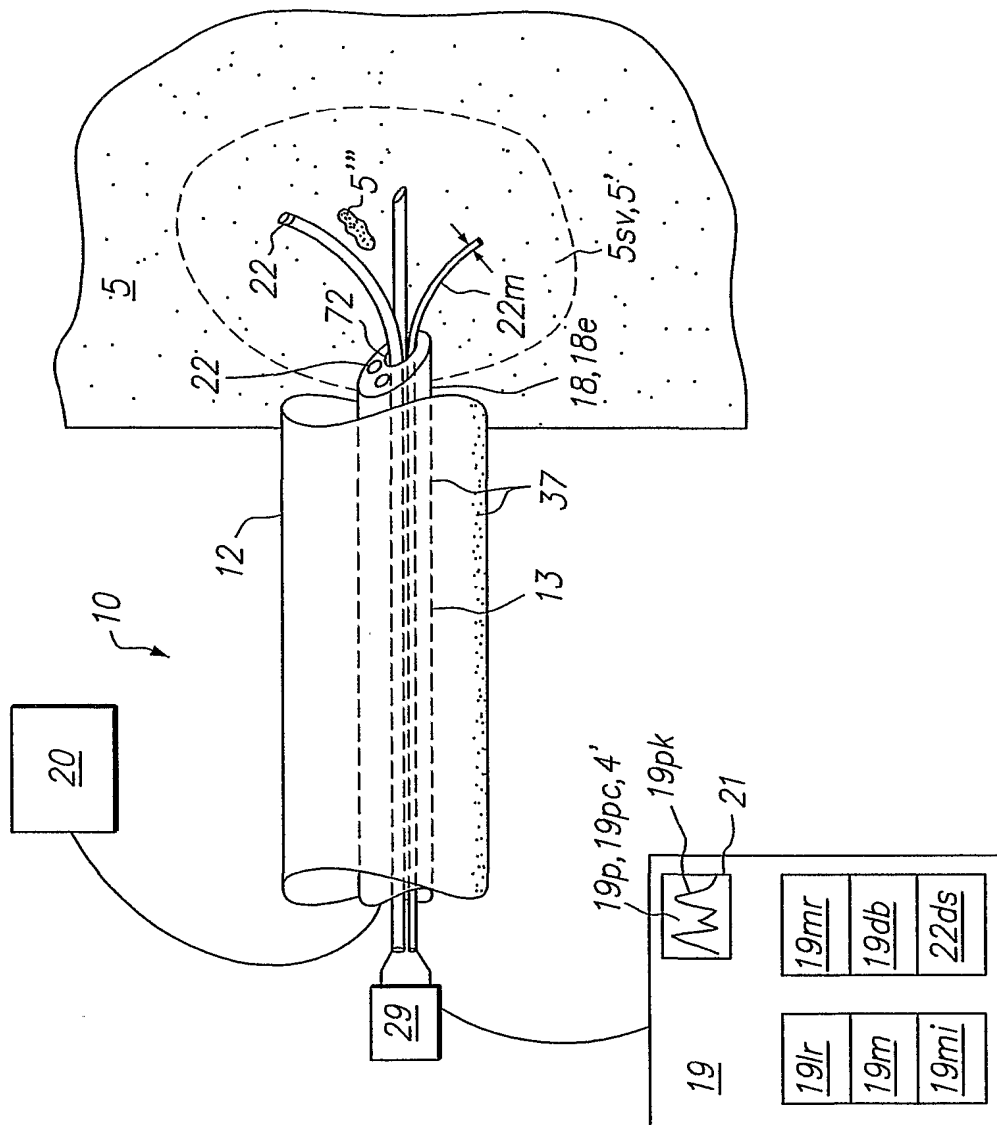


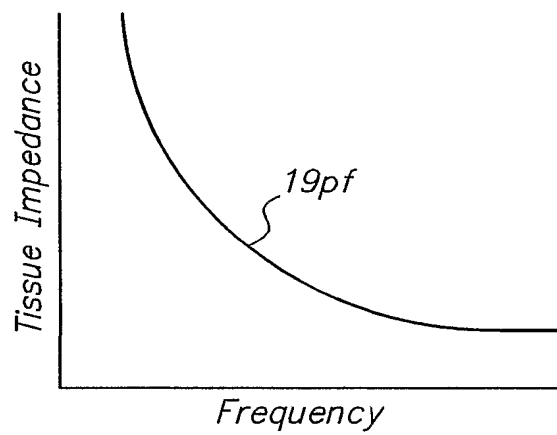
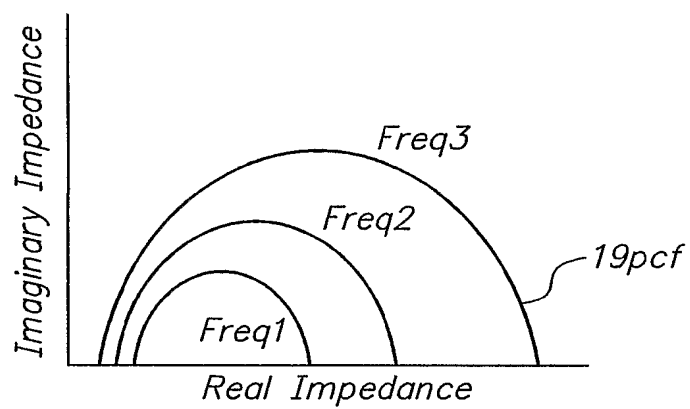
FIG. 5

6/26

FIG. 6



7/26

**FIG. 7A****FIG. 7B**

8/26

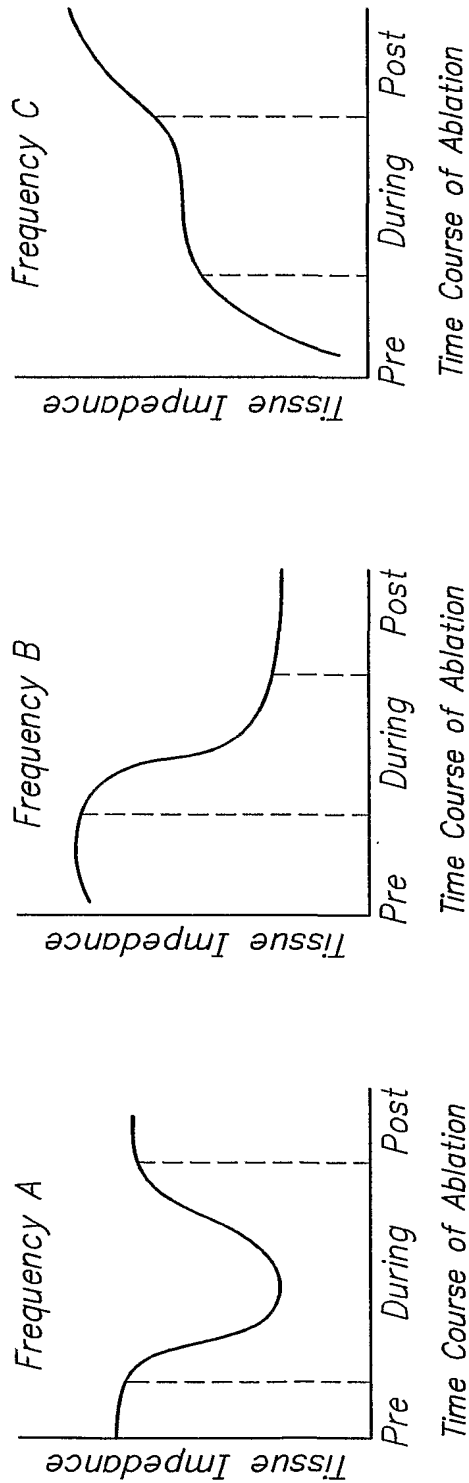


FIG. 8C

FIG. 8B

FIG. 8A

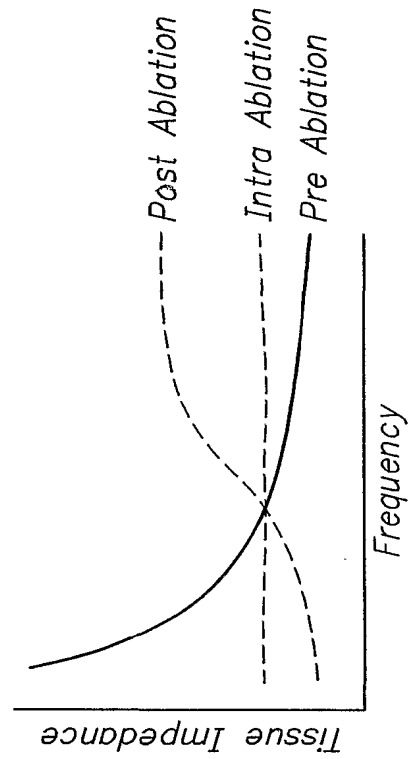
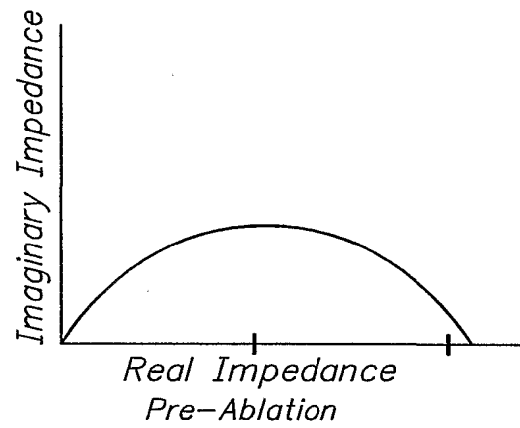
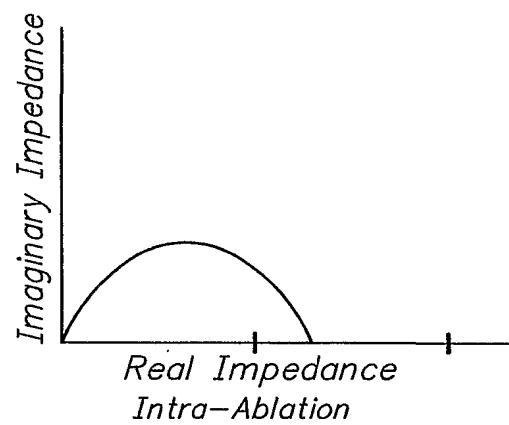
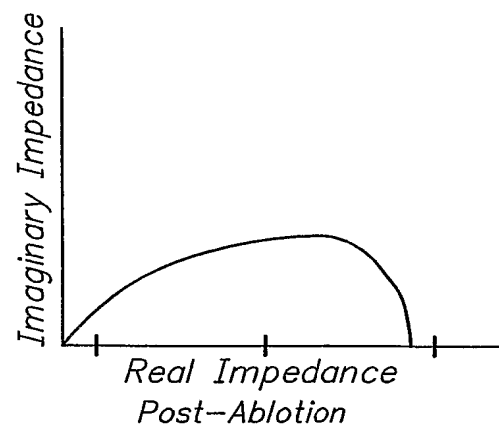
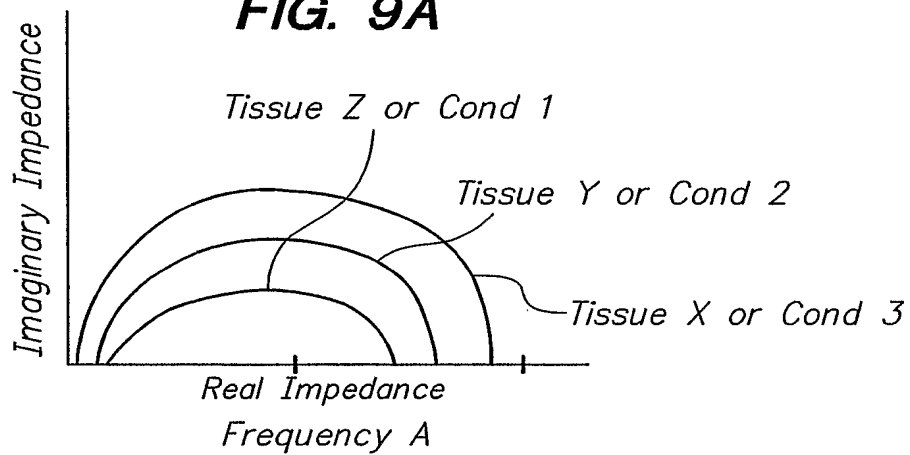
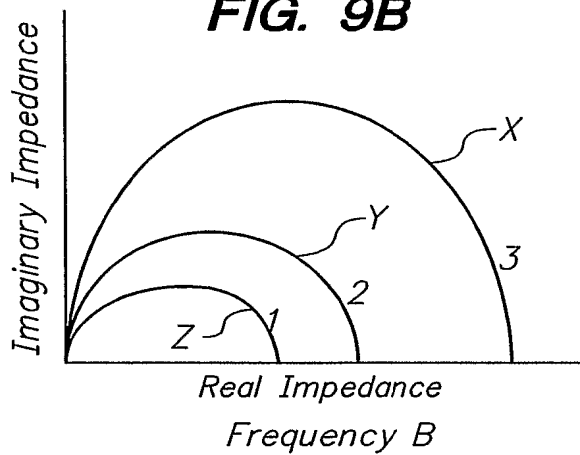
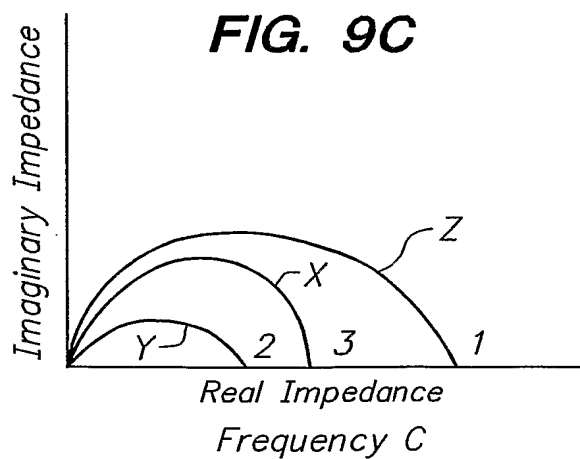


FIG. 8D

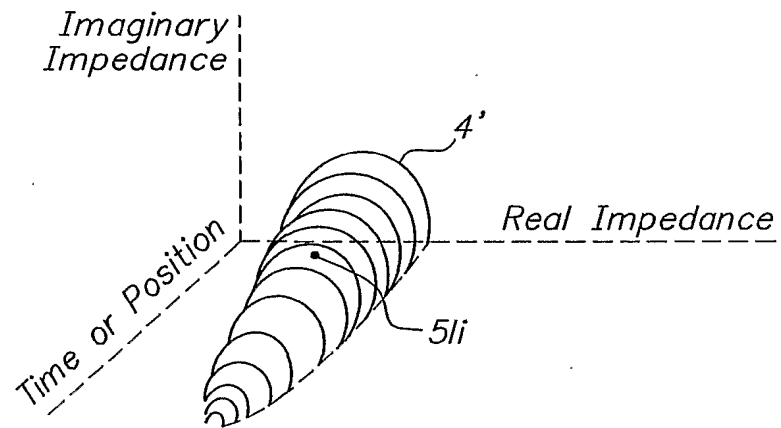
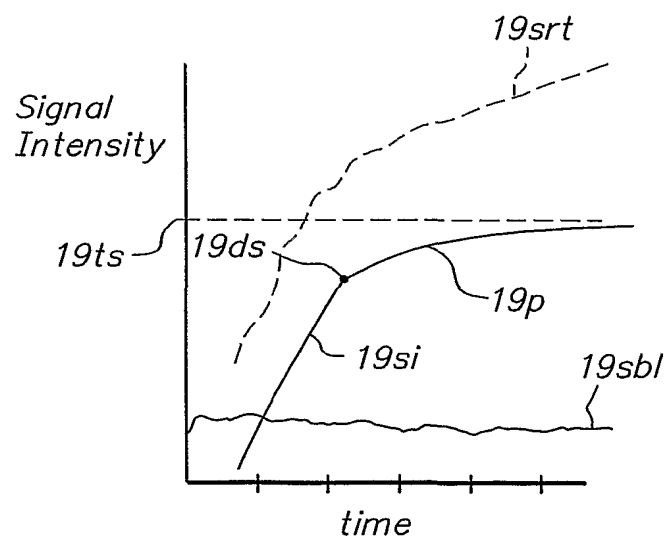
9/26

**FIG. 8E****FIG. 8F****FIG. 8G**

10/26

FIG. 9A**FIG. 9B****FIG. 9C**

11/26

FIG. 10**FIG. 11**

12/26

FIG. 12A

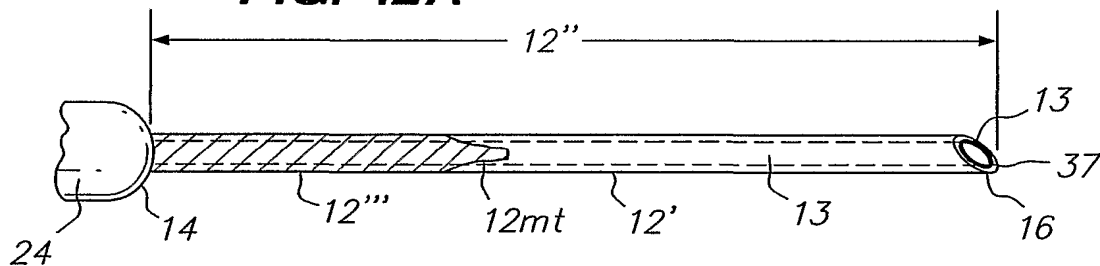


FIG. 12B

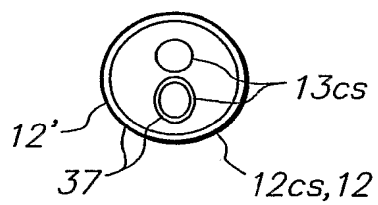


FIG. 12C

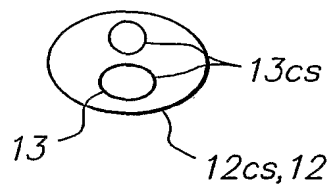
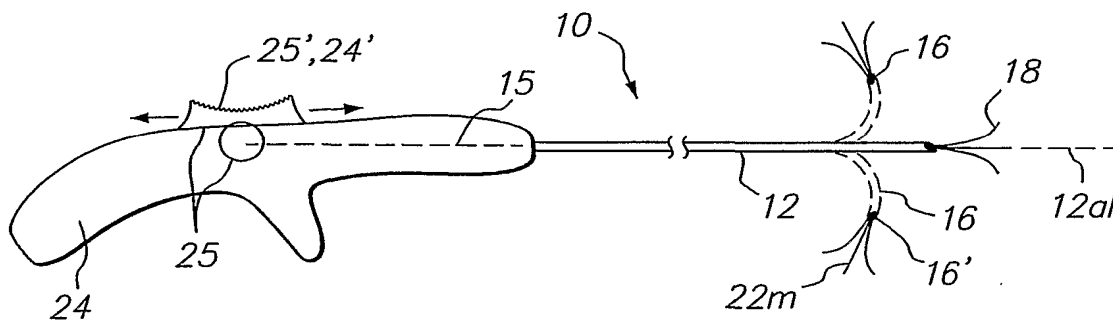
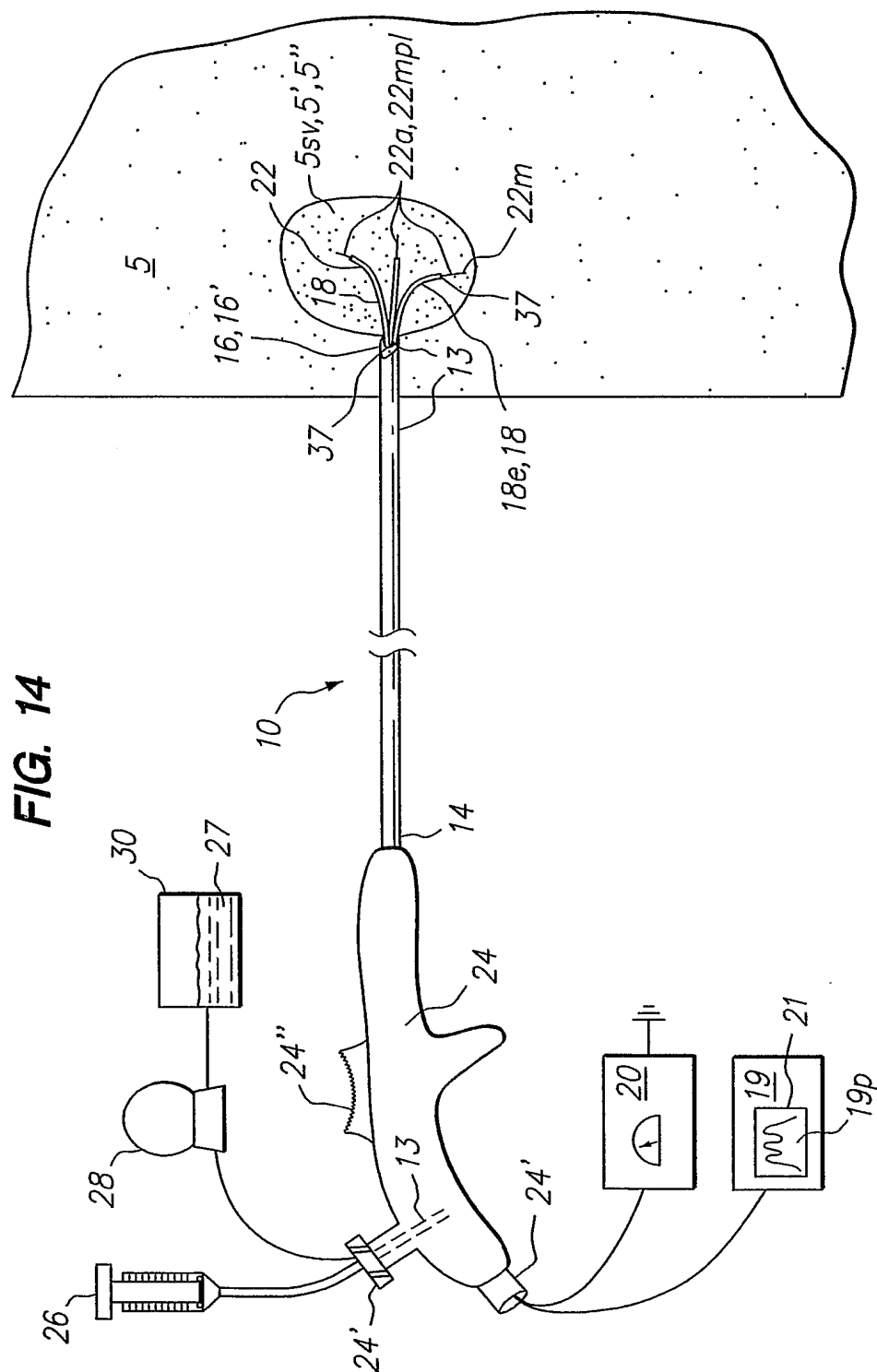


FIG. 13



13/26



14/26

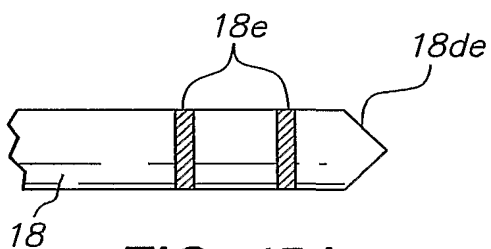


FIG. 15A

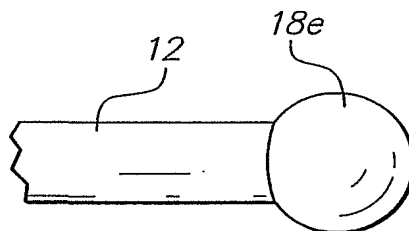


FIG. 15B

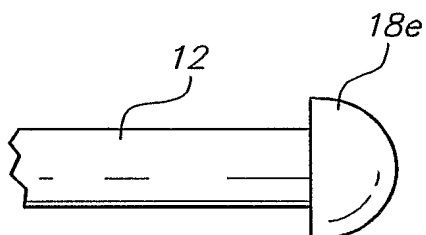


FIG. 15C

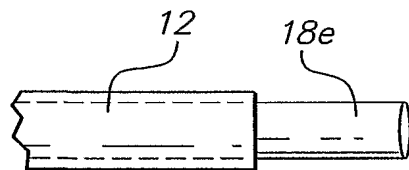


FIG. 15D

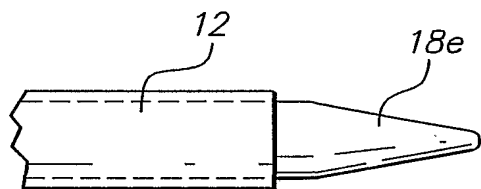


FIG. 15E

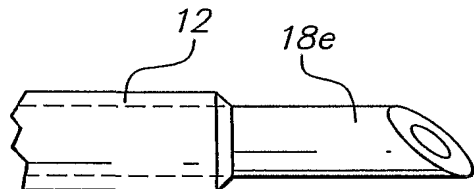


FIG. 15F

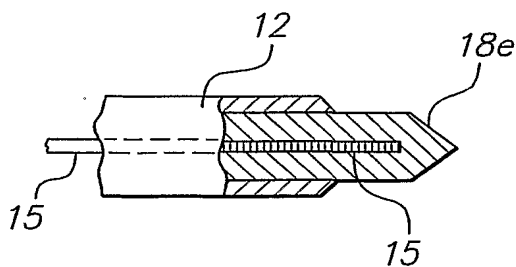


FIG. 15G

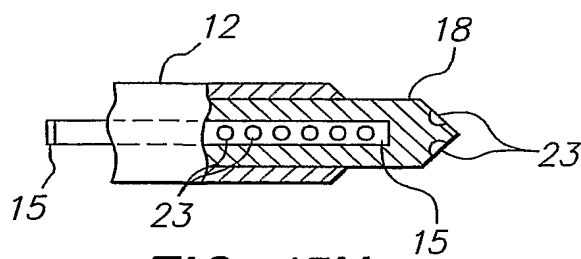
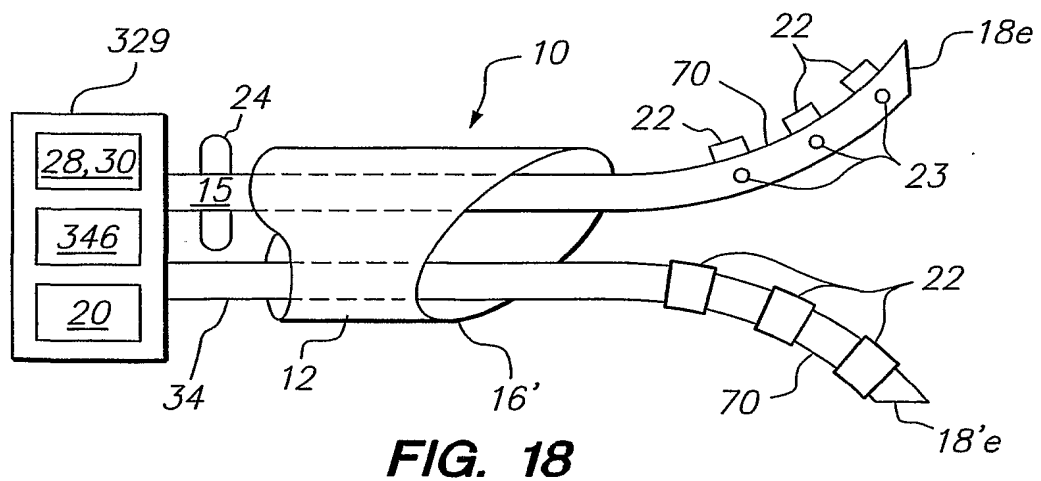
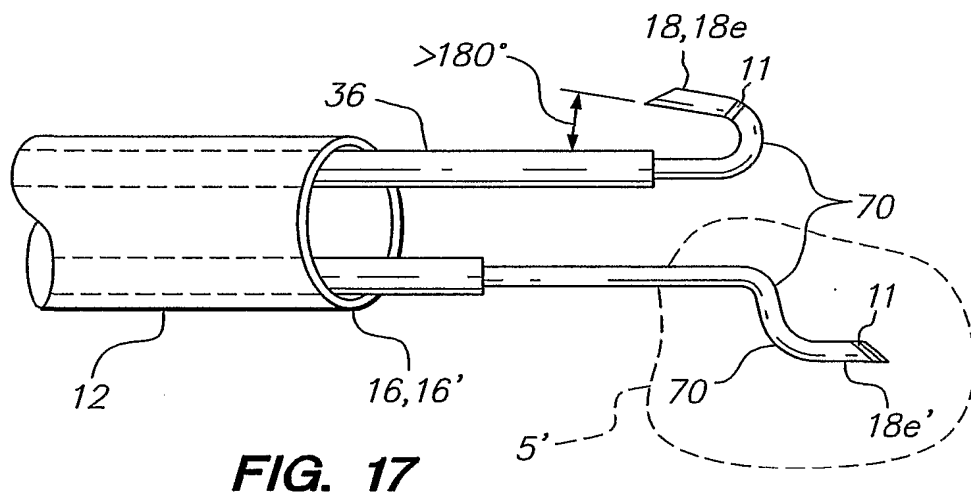
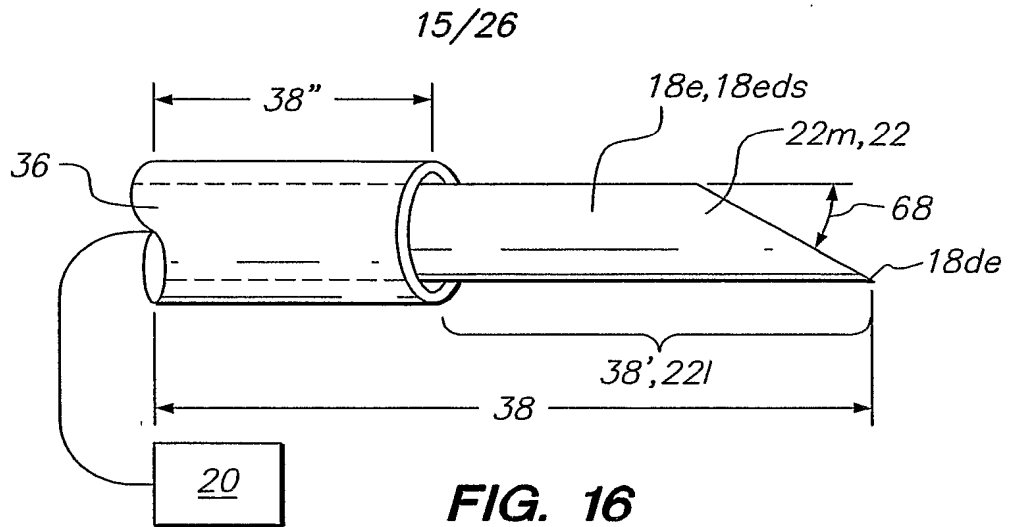
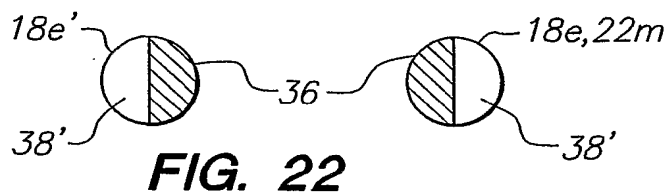
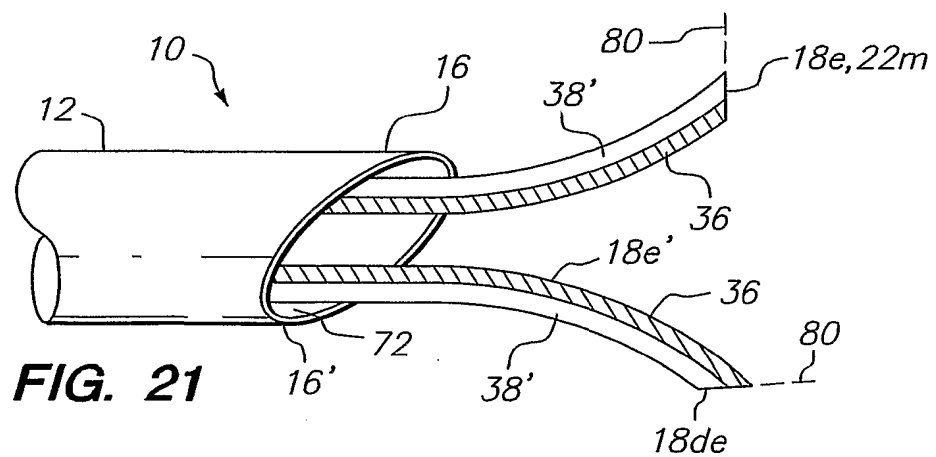
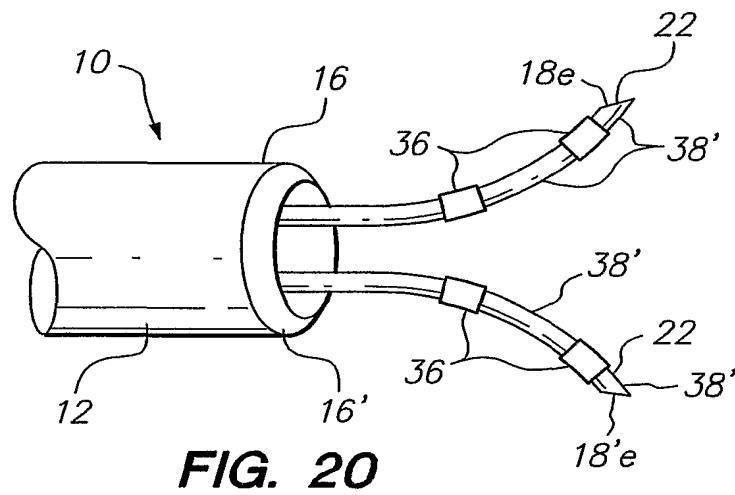
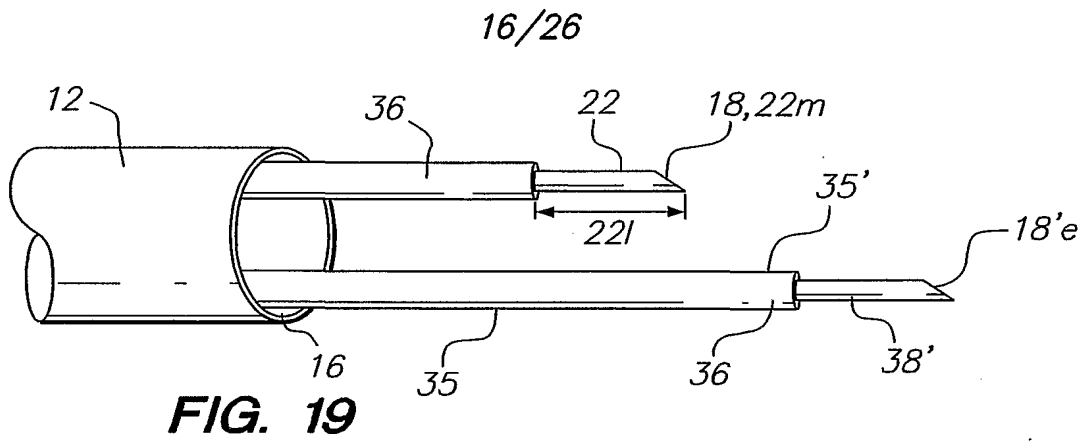


FIG. 15H





17/26

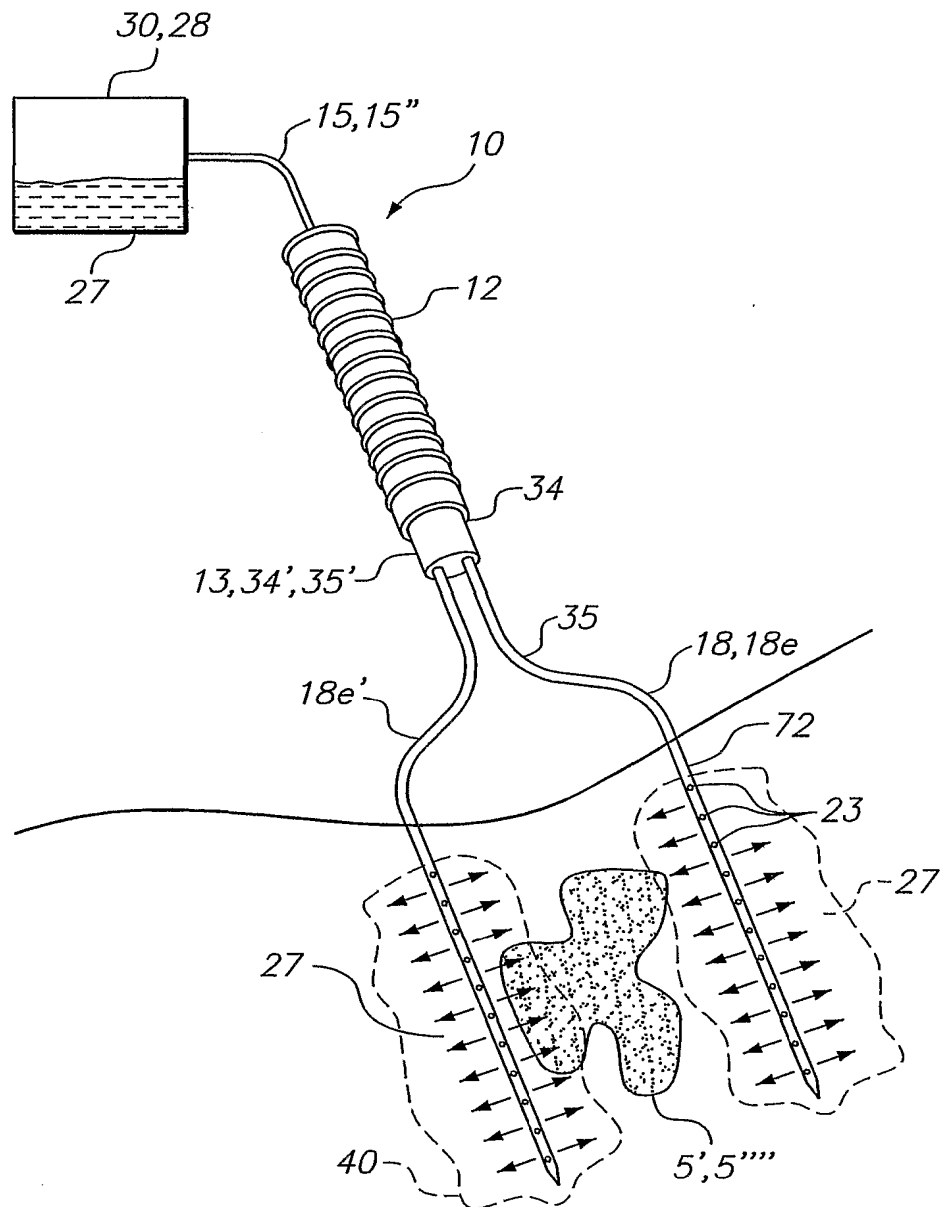
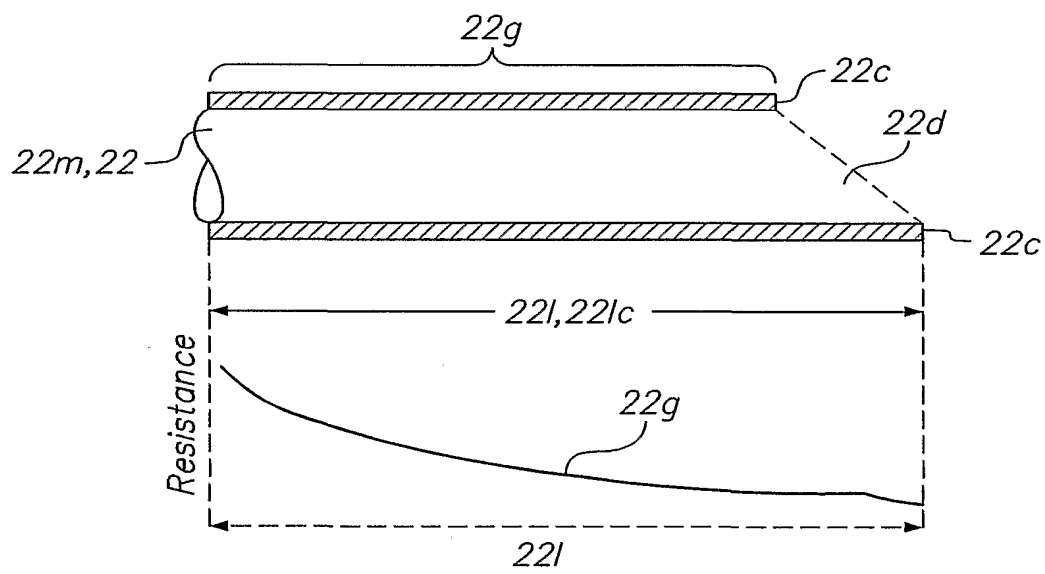


FIG. 23

18/26

FIG. 24

19/26

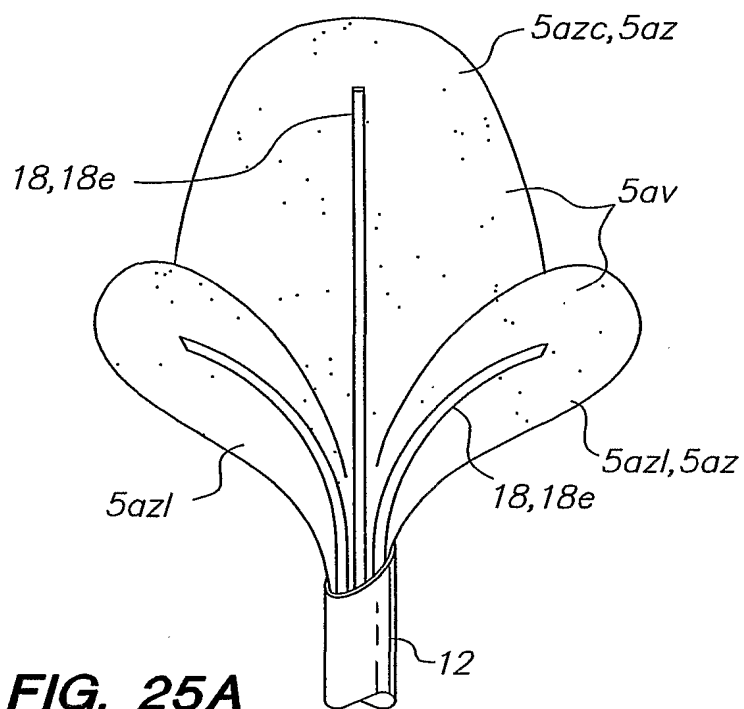


FIG. 25A

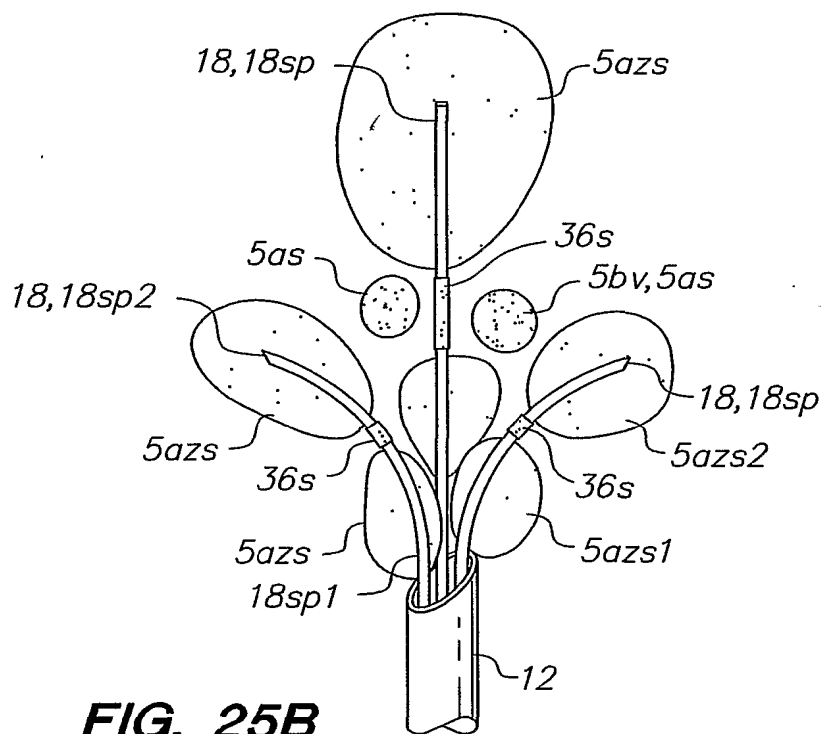


FIG. 25B

20/26

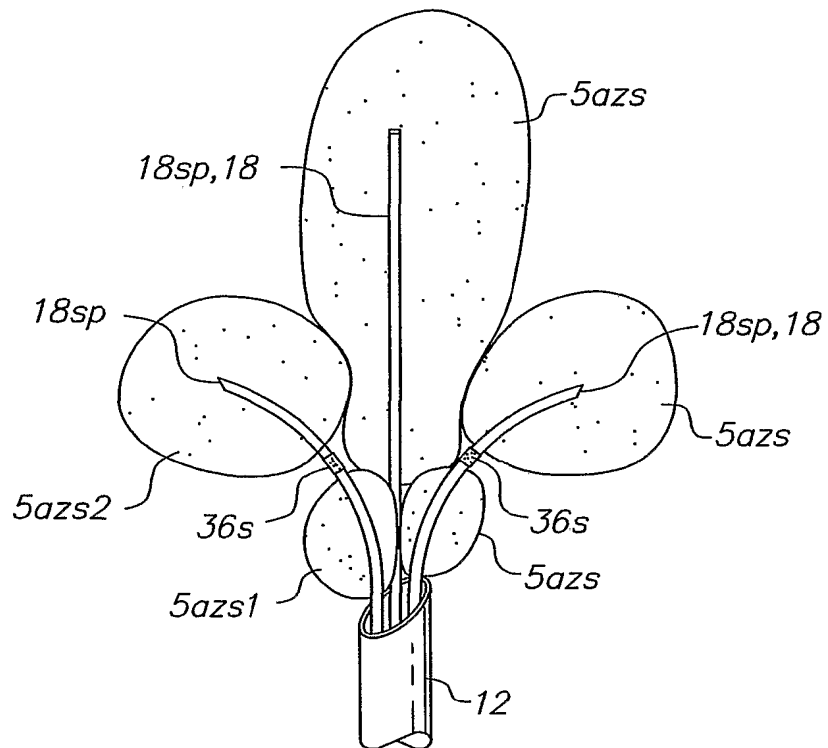


FIG. 25C

21/26

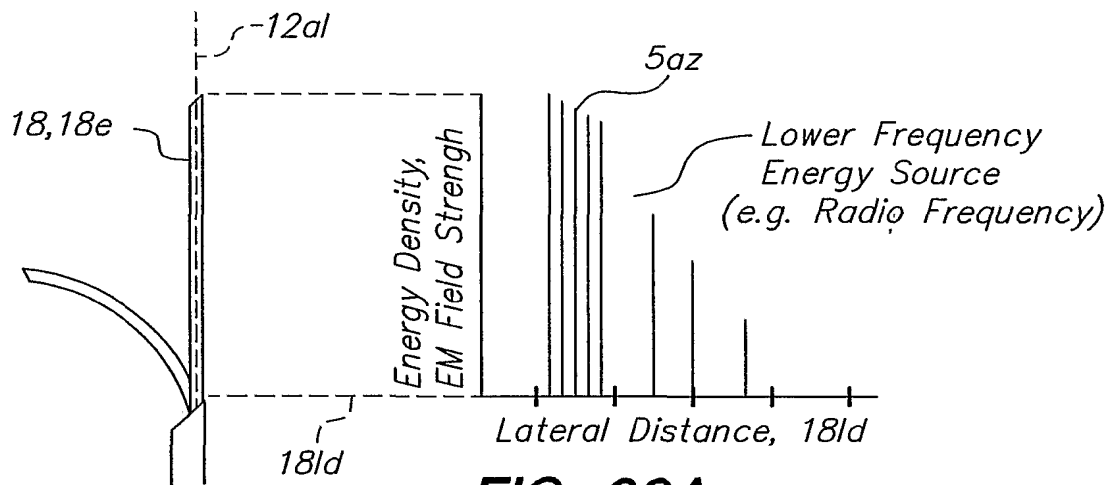


FIG. 26A

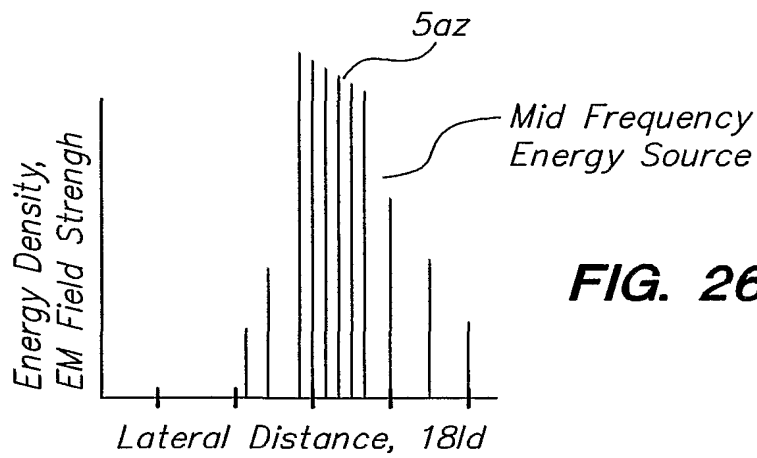


FIG. 26B

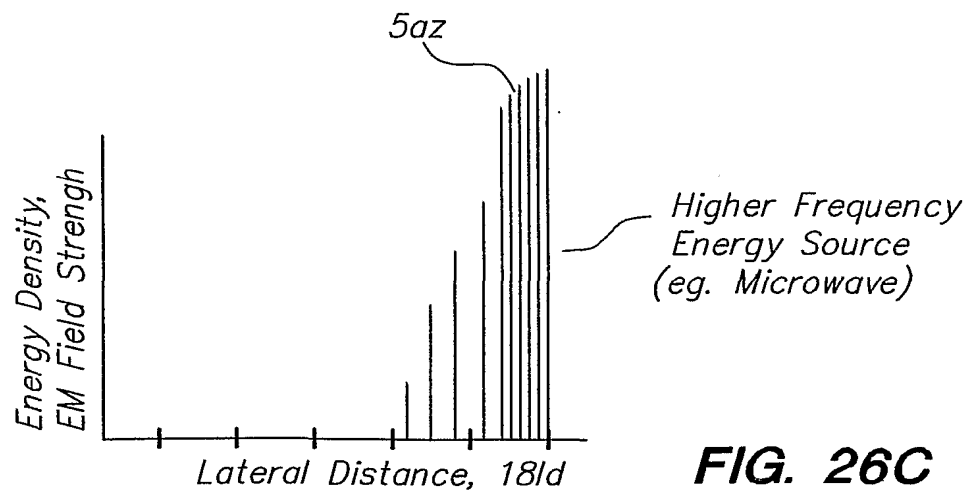


FIG. 26C

22/26

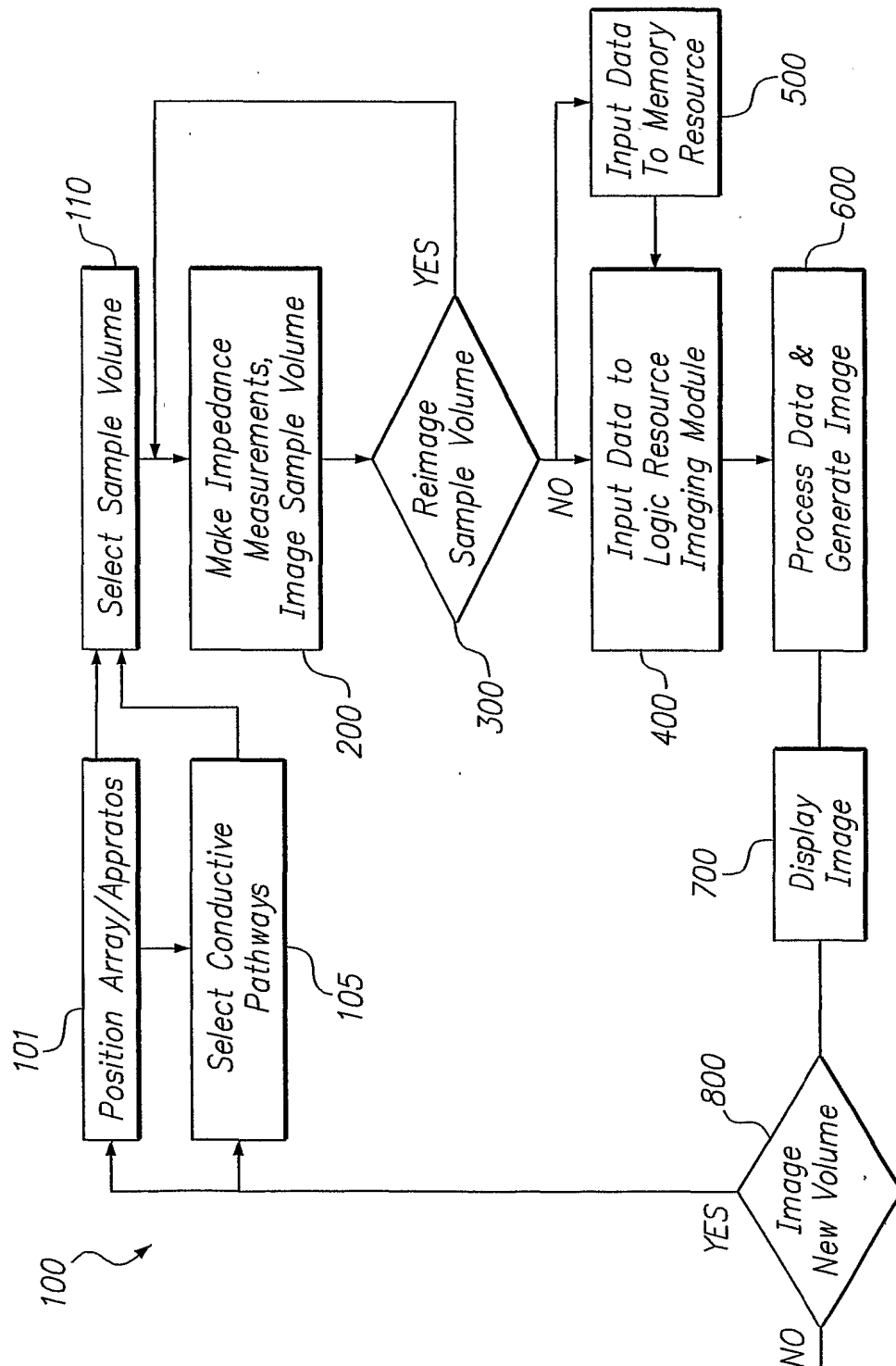


FIG. 27

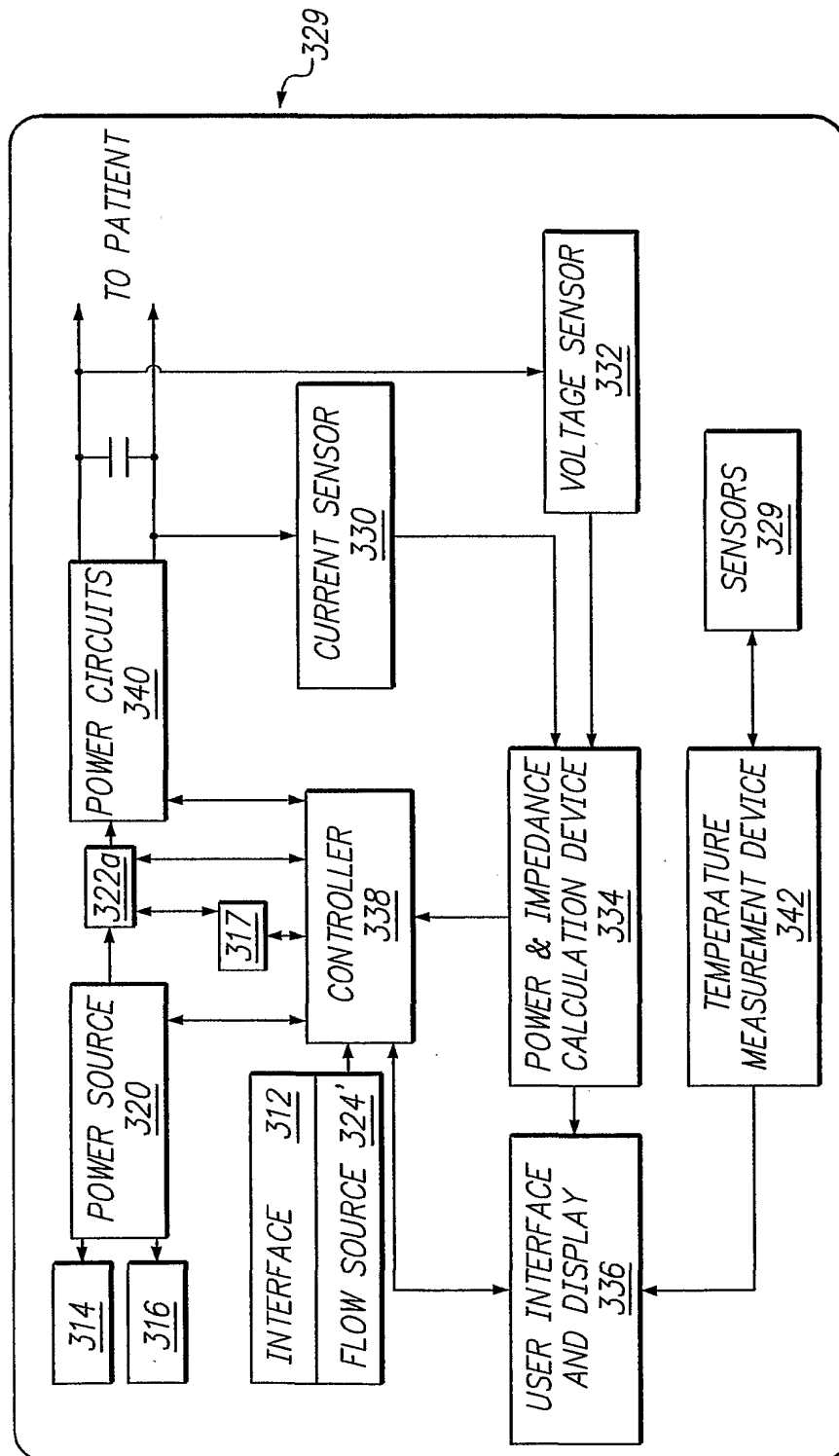
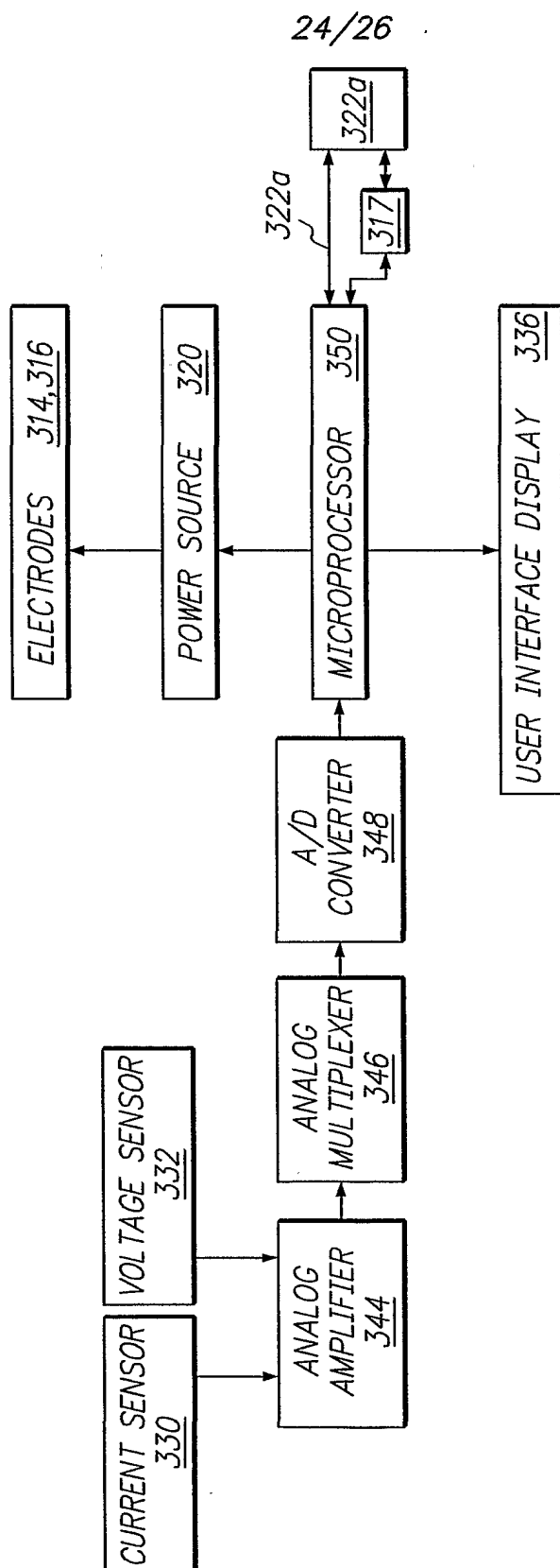
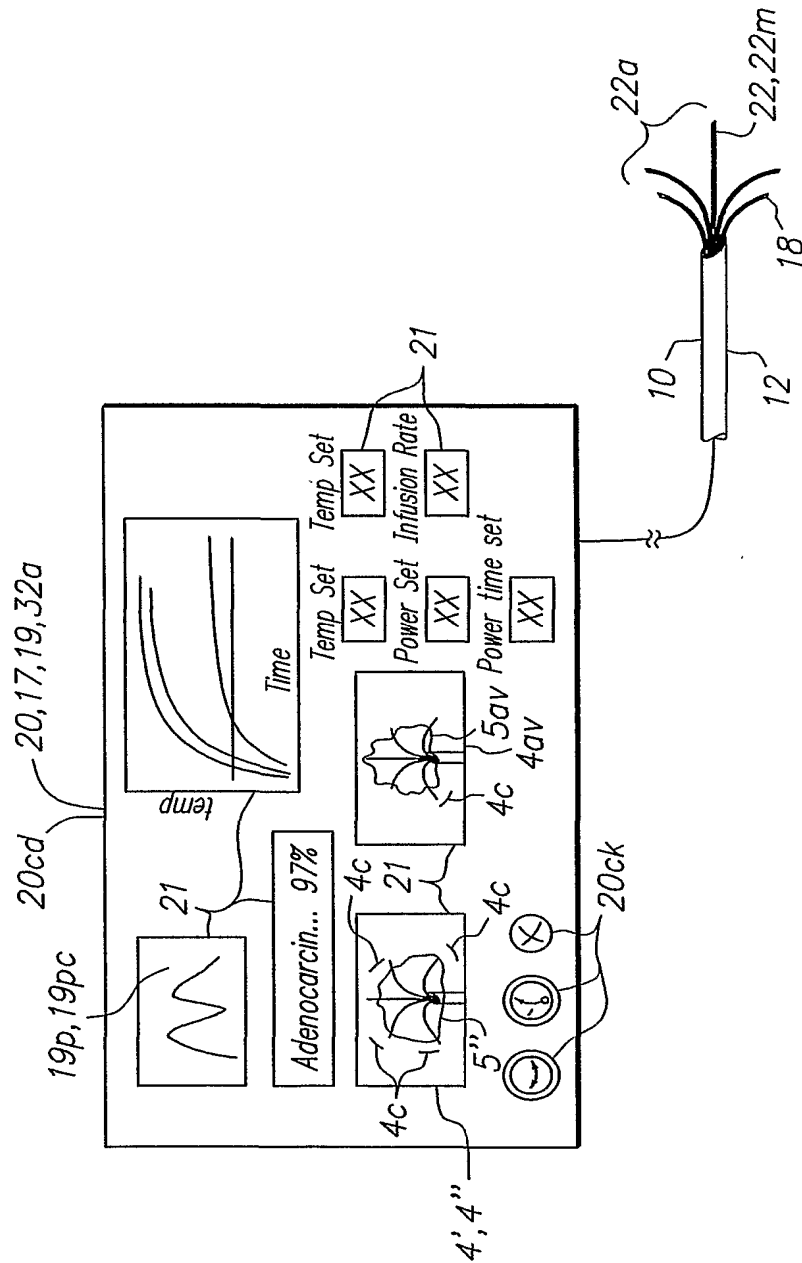


FIG. 28

**FIG. 29**

25/26

FIG. 30



26/26

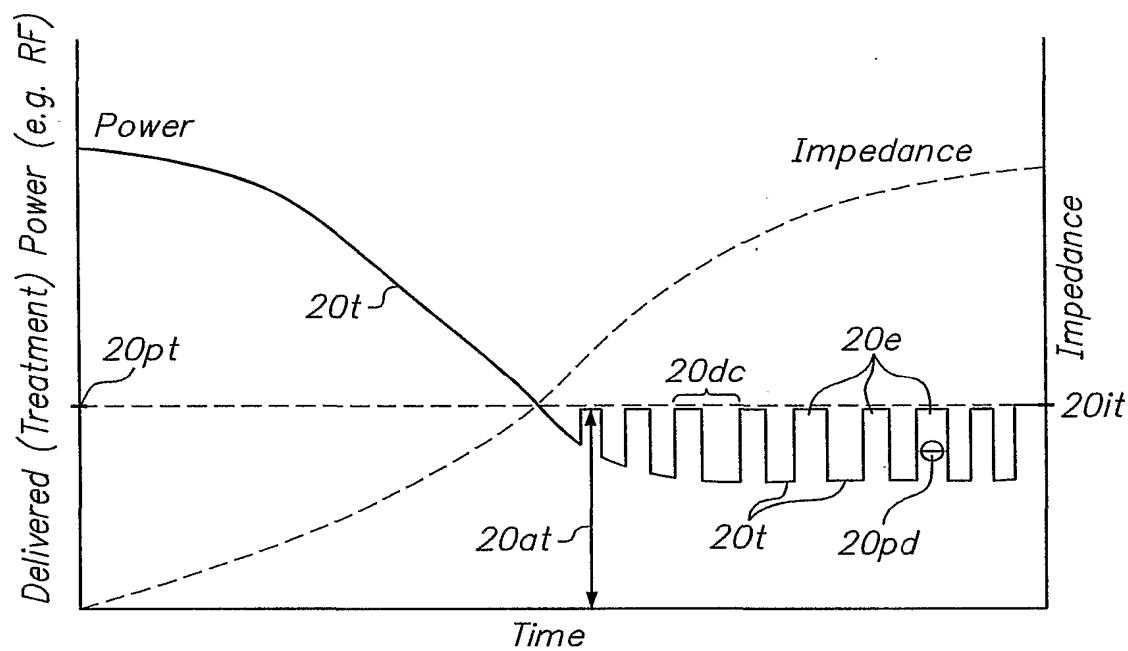


FIG. 31

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 01/23553

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61B18/14

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, PAJ, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 6 080 150 A (GOUGH EDWARD J) 27 June 2000 (2000-06-27) column 8, line 20-49; figures 7,9 ----	1, 2, 34, 35, 37
A	US 6 059 780 A (GOUGH EDWARD J ET AL) 9 May 2000 (2000-05-09) claim 20 ----	1
A	US 5 980 517 A (GOUGH EDWARD J) 9 November 1999 (1999-11-09) claim 18 ----	1
A	US 5 630 426 A (SHMULEWITZ ASCHER ET AL) 20 May 1997 (1997-05-20) see background of invention -----	1

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

A document defining the general state of the art which is not considered to be of particular relevance

E earlier document but published on or after the international filing date

L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

O document referring to an oral disclosure, use, exhibition or other means

P document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

* & * document member of the same patent family

Date of the actual completion of the international search

16 October 2001

Date of mailing of the international search report

24/10/2001

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Papone, F

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 01/23553

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
US 6080150	A	27-06-2000	US 6132425 A	17-10-2000
			US 5728143 A	17-03-1998
			US 5683384 A	04-11-1997
			TW 402498 B	21-08-2000
			US 5980517 A	09-11-1999
			US 6235023 B1	22-05-2001
			US 2001001819 A1	24-05-2001
			AU 1372099 A	24-05-1999
			WO 9922657 A1	14-05-1999
			AU 2254397 A	02-09-1997
			CN 1211171 A	17-03-1999
			EP 0883379 A1	16-12-1998
			JP 2000507844 T	27-06-2000
			WO 9729702 A1	21-08-1997
			US 5800484 A	01-09-1998
			US 6053937 A	25-04-2000
			AU 6851096 A	12-03-1997
			AU 6851296 A	12-03-1997
			AU 6898196 A	12-03-1997
			AU 7007996 A	12-03-1997
			EP 0957988 A2	24-11-1999
			EP 0851743 A1	08-07-1998
			EP 0850024 A1	01-07-1998
			JP 11511988 T	19-10-1999
			JP 2000500033 T	11-01-2000
			JP 11511991 T	19-10-1999
			JP 11511992 T	19-10-1999
			JP 2001231790 A	28-08-2001
			KR 243503 B1	02-03-2000
			KR 243744 B1	02-03-2000
			NL 1003793 C2	02-05-1997
			NL 1003793 A1	18-02-1997
			WO 9706739 A2	27-02-1997
			WO 9706740 A2	27-02-1997
			WO 9706855 A2	27-02-1997
			WO 9706857 A2	27-02-1997
			US 5863290 A	26-01-1999
			US 5782827 A	21-07-1998
			US 5735847 A	07-04-1998
			US 5672173 A	30-09-1997
			US 5672174 A	30-09-1997
			US 5810804 A	22-09-1998
			US 6071280 A	06-06-2000
			US 5928229 A	27-07-1999
			US 5951547 A	14-09-1999
			US 5925042 A	20-07-1999
			US 59138 A	
US 6059780	A	09-05-2000	US 5810804 A	22-09-1998
			US 5683384 A	04-11-1997
			AU 2327197 A	01-10-1997
			EP 0891158 A1	20-01-1999
			JP 2000506415 T	30-05-2000
			WO 9733524 A1	18-09-1997
			AU 6851096 A	12-03-1997
			AU 6851296 A	12-03-1997
			AU 6898196 A	12-03-1997
			AU 7007996 A	12-03-1997

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 01/23553

Patent document cited in search report	Publication date	Patent family member(s)	Publication date	
US 6059780	A	EP 0957988 A2	24-11-1999	
		EP 0851743 A1	08-07-1998	
		EP 0850024 A1	01-07-1998	
		JP 11511988 T	19-10-1999	
		JP 2000500033 T	11-01-2000	
		JP 11511991 T	19-10-1999	
		JP 11511992 T	19-10-1999	
		JP 2001231790 A	28-08-2001	
		KR 243503 B1	02-03-2000	
		KR 243744 B1	02-03-2000	
		NL 1003793 C2	02-05-1997	
		NL 1003793 A1	18-02-1997	
		US 6132425 A	17-10-2000	
		US 6080150 A	27-06-2000	
		US 5980517 A	09-11-1999	
		WO 9706739 A2	27-02-1997	
		WO 9706740 A2	27-02-1997	
		WO 9706855 A2	27-02-1997	
		WO 9706857 A2	27-02-1997	
		US 6235023 B1	22-05-2001	
		US 5863290 A	26-01-1999	
		US 5782827 A	21-07-1998	
		US 5735847 A	07-04-1998	
		US 5672173 A	30-09-1997	
		US 5672174 A	30-09-1997	
		US 5728143 A	17-03-1998	
		US 5800484 A	01-09-1998	
		US 2001001819 A1	24-05-2001	
		US 6071280 A	06-06-2000	
		US 5928229 A	27-07-1999	
		US 5951547 A	14-09-1999	
		US 5925042 A	20-07-1999	
		US 5913855 A	22-06-1999	
		US 6053937 A	25-04-2000	
		US 6090105 A	18-07-2000	
US 5980517	A	09-11-1999	US 6132425 A	17-10-2000
			US 5683384 A	04-11-1997
			TW 402498 B	21-08-2000
			US 6235023 B1	22-05-2001
			US 2001001819 A1	24-05-2001
			US 6080150 A	27-06-2000
			AU 1372099 A	24-05-1999
			WO 9922657 A1	14-05-1999
			AU 6851096 A	12-03-1997
			AU 6851296 A	12-03-1997
			AU 6898196 A	12-03-1997
			AU 7007996 A	12-03-1997
			EP 0957988 A2	24-11-1999
			EP 0851743 A1	08-07-1998
			EP 0850024 A1	01-07-1998
			JP 11511988 T	19-10-1999
			JP 2000500033 T	11-01-2000
			JP 11511991 T	19-10-1999
			JP 11511992 T	19-10-1999
			JP 2001231790 A	28-08-2001
			KR 243503 B1	02-03-2000
			KR 243744 B1	02-03-2000

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 01/23553

Patent document cited in search report	Publication date	Patent family member(s)	Publication date	
US 5980517	A	NL 1003793 C2	02-05-1997	
		NL 1003793 A1	18-02-1997	
		WO 9706739 A2	27-02-1997	
		WO 9706740 A2	27-02-1997	
		WO 9706855 A2	27-02-1997	
		WO 9706857 A2	27-02-1997	
		US 5863290 A	26-01-1999	
		US 5782827 A	21-07-1998	
		US 5735847 A	07-04-1998	
		US 5672173 A	30-09-1997	
		US 5672174 A	30-09-1997	
		US 5728143 A	17-03-1998	
		US 5810804 A	22-09-1998	
		US 5800484 A	01-09-1998	
		US 6071280 A	06-06-2000	
		US 5928229 A	27-07-1999	
		US 5951547 A	14-09-1999	
		US 5925042 A	20-07-1999	
		US 5913855 A	22-06-1999	
		US 6053937 A	25-04-2000	
		US 6059780 A	09-05-2000	
		US 6090105 A	18-07-2000	
US 5630426	A	20-05-1997	AU 696729 B2	17-09-1998
			AU 5180196 A	23-09-1996
			CA 2214574 A1	12-09-1996
			EP 0813387 A1	29-12-1997
			WO 9627327 A1	12-09-1996
			US 5928159 A	27-07-1999
			US 5947964 A	07-09-1999
			US 6106524 A	22-08-2000